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(54) Title: 83 HUMAN SECRETED PROTEINS

(57) Abstract: The present invention relates to novel human secreted proteins and isolated nucleic acids containing the coding regions of the genes encoding such proteins. Also provided are vectors, host cells, antibodies, and recombinant methods for producing human secreted proteins. The invention further relates to diagnostic and therapeutic methods useful for diagnosing and treating diseases, disorders, and/or conditions related to those novel human secreted proteins.

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83 Human Secreted Proteins

Field of the Invention

This invention relates to newly identified polynucleotides, polypeptides encoded by these polynucleotides, antibodies that bind these polypeptides, uses of such polynucleotides, polypeptides, and antibodies, and their production.

Background of the Invention

Unlike bacterium, which exist as a single compartment surrounded by a membrane, human cells and other eucaryotes are subdivided by membranes into many functionally distinct compartments. Each membrane-bounded compartment, or organelle, contains different proteins essential for the function of the organelle. The cell uses "sorting signals," which are amino acid motifs located within the protein, to target proteins to particular cellular organelles.

One type of sorting signal, called a signal sequence, a signal peptide, or a leader sequence, directs a class of proteins to an organelle called the endoplasmic reticulum (ER). The ER separates the membrane-bounded proteins from all other types of proteins. Once localized to the ER, both groups of proteins can be further directed to another organelle called the Golgi apparatus. Here, the Golgi distributes the proteins to vesicles, including secretory vesicles, the cell membrane, lysosomes, and the other organelles.

Proteins targeted to the ER by a signal sequence can be released into the extracellular space as a secreted protein. For example, vesicles containing secreted proteins can fuse with the cell membrane and release their contents into the extracellular space - a process called exocytosis. Exocytosis can occur constitutively or after receipt of a triggering signal. In the latter case, the proteins are stored in secretory vesicles (or secretory granules) until exocytosis is triggered. Similarly, proteins residing on the cell membrane can also be secreted into the extracellular space by proteolytic cleavage of a "linker" holding the protein to the membrane.

Despite the great progress made in recent years, only a small number of genes encoding human secreted proteins have been identified. These secreted proteins include the commercially valuable human insulin, interferon, Factor VIII, human

growth hormone, tissue plasminogen activator, and erythropoeitin. Thus, in light of the pervasive role of secreted proteins in human physiology, a need exists for identifying and characterizing novel human secreted proteins and the genes that encode them. This knowledge will allow one to detect, to treat, and to prevent medical diseases, disorders, and/or conditions by using secreted proteins or the genes that encode them.

Summary of the Invention

The present invention relates to novel polynucleotides and the encoded polypeptides. Moreover, the present invention relates to vectors, host cells, antibodies, and recombinant and synthetic methods for producing the polypeptides and polynucleotides. Also provided are diagnostic methods for detecting diseases, disorders, and/or conditions related to the polypeptides and polynucleotides, and therapeutic methods for treating such diseases, disorders, and/or conditions. The invention further relates to screening methods for identifying binding partners of the polypeptides.

In other embodiments, the present invention encompasses methods of preventing, treating, diagnosing, or ameliorating a disease or disorder. In preferred embodiments, the present invention encompasses a method of treating a disease or disorder listed in the "Preferred Indications" column of Table 1C; comprising administering to a patient in which such treatment, prevention, or amelioration is desired a protein, nucleic acid, or antibody of the invention (or fragment or variant thereof) represented by Table 1A and Table 1C (in the same row as the disease or disorder to be treated is listed in the "Preferred Indications" column of Table 1C) in an amount effective to treat, prevent, or ameliorate the disease or disorder.

In another embodiment, the present invention also encompasses methods of preventing, treating, diagnosing, or ameliorating a disease or disorder listed in the "Preferred Indications" column of Table 1C; comprising administering to a patient combinations of the proteins, nucleic acids, or antibodies of the invention (or fragments or variants thereof) as represented by Table 1A and Table 1C.

Detailed Description

Tables

Table 1A summarizes information concerning certain polynucleotides and polypeptides of the invention. The first column provides the gene number in the application for each clone identifier. The second column provides a unique clone identifier, "cDNA clone ID", for a cDNA clone related to each contig sequence disclosed in Table 1A. Third column, the cDNA Clones identified in the second column were deposited as indicated (i.e. by ATCC Deposit No:Z and deposit date) Some of the deposits contain multiple different clones corresponding to the same gene. In the fourth column, "Vector" refers to the type of vector contained in the corresponding cDNA Clone identified in the second column. In the fifth column, the nucleotide sequence identified as "NT SEQ ID NO:X" was assembled from partially homologous ("overlapping") sequences obtained from the corresponding cDNA clone identified in the second column and, in some cases, from additional related cDNA clones. The overlapping sequences were assembled into a single contiguous sequence of high redundancy (usually three to five overlapping sequences at each nucleotide position), resulting in a final sequence identified as SEQ ID NO:X. In the sixth column, "Total NT Seq." refers to the total number of nucleotides in the contig sequence identified as SEQ ID NO:X." The deposited clone may contain all or most of these sequences, reflected by the nucleotide position indicated as "5' NT of Clone Seq." (seventh column) and the "3' NT of Clone Seq." (eighth column) of SEQ ID NO:X. In the ninth column, the nucleotide position of SEQ ID NO:X of the putative start codon (methionine) is identified as "5' NT of Start Codon." Similarly , in column ten, the nucleotide position of SEQ ID NO:X of the predicted signal sequence is identified as "5' NT of First AA of Signal Pep." In the eleventh column, the translated amino acid sequence, as shown in the sequence listing, is identified as "AA SEQ ID NO:Y," although other reading frames can also be routinely translated using known molecular biology techniques. The polypeptides produced by these alternative open reading frames are specifically contemplated by the present invention.

In the twelfth and thirteenth columns of Table 1A, the first and last amino acid position of SEQ ID NO:Y of the predicted signal peptide is identified as "First AA of

Sig Pep" and "Last AA of Sig Pep.," respectively. In the fourteenth column, the predicted first amino acid position of SEQ ID NO:Y of the secreted portion is identified as "Predicted First AA of Secreted Portion". The amino acid position of SEQ ID NO:Y of the last amino acid encoded by the open reading frame is identified in the fifteenth column as "Last AA of ORF".

SEQ ID NO:X (where X may be any of the polynucleotide sequences disclosed in the sequence listing) and the translated SEQ ID NO:Y (where Y may be any of the polypeptide sequences disclosed in the sequence listing) are sufficiently accurate and otherwise suitable for a variety of uses well known in the art and described further below. For instance, SEQ ID NO:X is useful for designing nucleic acid hybridization probes that will detect nucleic acid sequences contained in SEQ ID NO:X or the cDNA contained in the deposited clone. These probes will also hybridize to nucleic acid molecules in biological samples, thereby enabling a variety of forensic and diagnostic methods of the invention. Similarly, polypeptides identified from SEQ ID NO:Y may be used, for example, to generate antibodies which bind specifically to proteins containing the polypeptides and the secreted proteins encoded by the cDNA clones identified in Table 1A and/or elsewhere herein.

Nevertheless, DNA sequences generated by sequencing reactions can contain sequencing errors. The errors exist as misidentified nucleotides, or as insertions or deletions of nucleotides in the generated DNA sequence. The erroneously inserted or deleted nucleotides cause frame shifts in the reading frames of the predicted amino acid sequence. In these cases, the predicted amino acid sequence diverges from the actual amino acid sequence, even though the generated DNA sequence may be greater than 99.9% identical to the actual DNA sequence (for example, one base insertion or deletion in an open reading frame of over 1000 bases).

Accordingly, for those applications requiring precision in the nucleotide sequence or the amino acid sequence, the present invention provides not only the generated nucleotide sequence identified as SEQ ID NO:X, and the predicted translated amino acid sequence identified as SEQ ID NO:Y, but also a sample of plasmid DNA containing a human cDNA of the invention deposited with the ATCC, as set forth in Table 1A. The nucleotide sequence of each deposited plasmid can

readily be determined by sequencing the deposited plasmid in accordance with known methods.

The predicted amino acid sequence can then be verified from such deposits. Moreover, the amino acid sequence of the protein encoded by a particular plasmid can also be directly determined by peptide sequencing or by expressing the protein in a suitable host cell containing the deposited human cDNA, collecting the protein, and determining its sequence.

Also provided in Table 1A is the name of the vector which contains the cDNA plasmid. Each vector is routinely used in the art. The following additional information is provided for convenience.

Vectors Lambda Zap (U.S. Patent Nos. 5,128,256 and 5,286,636), Uni-Zap XR (U.S. Patent Nos. 5,128, 256 and 5,286,636), Zap Express (U.S. Patent Nos. 5,128,256 and 5,286,636), pBluescript (pBS) (Short, J. M. et al., *Nucleic Acids Res. 16:*7583-7600 (1988); Alting-Mees, M. A. and Short, J. M., *Nucleic Acids Res. 17:*9494 (1989)) and pBK (Alting-Mees, M. A. et al., *Strategies 5:*58-61 (1992)) are commercially available from Stratagene Cloning Systems, Inc., 11011 N. Torrey Pines Road, La Jolla, CA, 92037. pBS contains an ampicillin resistance gene and pBK contains a neomycin resistance gene. Phagemid pBS may be excised from the Lambda Zap and Uni-Zap XR vectors, and phagemid pBK may be excised from the Zap Express vector. Both phagemids may be transformed into *E. coli* strain XL-1 Blue, also available from Stratagene.

Vectors pSport1, pCMVSport 1.0, pCMVSport 2.0 and pCMVSport 3.0, were obtained from Life Technologies, Inc., P. O. Box 6009, Gaithersburg, MD 20897. All Sport vectors contain an ampicillin resistance gene and may be transformed into *E. coli* strain DH10B, also available from Life Technologies. See, for instance, Gruber, C. E., et al., *Focus 15:*59 (1993). Vector lafmid BA (Bento Soares, Columbia University, New York, NY) contains an ampicillin resistance gene and can be transformed into *E. coli* strain XL-1 Blue. Vector pCR®2.1, which is available from Invitrogen, 1600 Faraday Avenue, Carlsbad, CA 92008, contains an ampicillin resistance gene and may be transformed into *E. coli* strain DH10B, available from Life Technologies. See, for instance, Clark, J. M., *Nuc. Acids Res. 16:*9677-9686 (1988) and Mead, D. *et al., Bio/Technology 9:* (1991).

The present invention also relates to the genes corresponding to SEQ ID NO:X, SEQ ID NO:Y, and/or a deposited cDNA (cDNA Clone ID). The corresponding gene can be isolated in accordance with known methods using the sequence information disclosed herein. Such methods include, but are not limited to, preparing probes or primers from the disclosed sequence and identifying or amplifying the corresponding gene from appropriate sources of genomic material.

Also provided in the present invention are allelic variants, orthologs, and/or species homologs. Procedures known in the art can be used to obtain full-length genes, allelic variants, splice variants, full-length coding portions, orthologs, and/or species homologs of genes corresponding to SEQ ID NO:X and SEQ ID NO:Y using information from the sequences disclosed herein or the clones deposited with the ATCC. For example, allelic variants and/or species homologs may be isolated and identified by making suitable probes or primers from the sequences provided herein and screening a suitable nucleic acid source for allelic variants and/or the desired homologue.

The present invention provides a polynucleotide comprising, or alternatively consisting of, the nucleic acid sequence of SEQ ID NO:X and/or a cDNA contained in ATCC deposit Z. The present invention also provides a polypeptide comprising, or alternatively, consisting of, the polypeptide sequence of SEQ ID NO:Y, a polypeptide encoded by SEQ ID NO:X, and/or a polypeptide encoded by a cDNA contained in ATCC deposit Z. Polynucleotides encoding a polypeptide comprising, or alternatively consisting of the polypeptide sequence of SEQ ID NO:Y, a polypeptide encoded by SEQ ID NO:X and/or a polypeptide encoded by the cDNA contained in ATCC deposit Z, are also encompassed by the invention. The present invention further encompasses a polynucleotide comprising, or alternatively consisting of the complement of the nucleic acid sequence of SEQ ID NO:X, and/or the complement of the coding strand of the cDNA contained in ATCC deposit Z.

Table 1B summarizes some of the polynucleotides encompassed by the invention (including cDNA clones related to the sequences (Clone ID NO.), contig sequences (contig identifier "Contig ID:") and contig nucleotide sequence identifier (SEQ ID NO:X)) and further summarizes certain characteristics of these

polynucleotides and the polypeptides encoded thereby. The first column provides the gene number in the application for each clone identifier. The second column provides a unique clone identifier, "Clone ID NO", for a cDNA clone related to each contig sequence disclosed in Table 1A and/or 1B. The third column provides a unique contig identifier, "Contig ID:" for each of the contig sequences disclosed in Table 1B. The fourth column provides the sequence identifier, "SEQ ID NO:X", for each of the contig sequences disclosed in Table 1A and/or 1B. The fifth column, "ORF (From-To)", provides the location (i.e., nucleotide position numbers) within the polynucleotide sequence of SEQ ID NO:X that delineate the preferred open reading frame (ORF) that encodes the amino acid sequence shown in the sequence listing and referenced in Table 1B as SEQ ID NO:Y (column 6). Column 7 lists residues comprising predicted epitopes in the polypeptides encoded by each of the preferred ORFs (SEQ ID NO:Y). Identification of potential immunogenic regions was performed according to the method of Jameson and Wolf (CABIOS, 4; 181-186 (1988)); specifically, the Genetics Computer Group (GCG) implementation of this algorithm, embodied in the program PEPTIDESTRUCTURE (Wisconsin Package v10.0, Genetics Computer Group (GCG), Madison, Wisc.). This method returns a measure of the probability that a given residue is found on the surface of the protein. Regions where the antigenic index score is greater than 0.9 over at least 6 amino acids are indicated in Table 1B as "Predicted Epitopes". In particular embodiments, polypeptides of the invention comprise, or alternatively consist of, one, two, three, four, five or more of the predicted epitopes described in Table 1B. It will be appreciated that depending on the analytical criteria used to predict antigenic determinants, the exact address of the determinant may vary slightly. Column 8, "Tissue Distribution" shows the expression profile of tissue, cells, and/or cell line libraries which express the polynucleotides of the invention. The first number in column 8 (preceding the colon), represents the tissue/cell source identifier code corresponding to the key provided in Table 4. Expression of these polynucleotides was not observed in the other tissues and/or cell libraries tested. For those identifier codes in which the first two letters are not "AR", the second number in column 8 (following the colon), represents the number of times a sequence corresponding to the reference polynucleotide sequence (e.g., SEQ ID NO:X) was identified in the

corresponding tissue/cell source. Those tissue/cell source identifier codes in which the first two letters are "AR" designate information generated using DNA array technology. Utilizing this technology, cDNAs were amplified by PCR and then transferred, in duplicate, onto the array. Gene expression was assayed through hybridization of first strand cDNA probes to the DNA array. cDNA probes were generated from total RNA extracted from a variety of different tissues and cell lines. Probe synthesis was performed in the presence of ^{33}P dCTP, using oligo(dT) to prime reverse transcription. After hybridization, high stringency washing conditions were employed to remove non-specific hybrids from the array. The remaining signal, emanating from each gene target, was measured using a Phosphorimager. Gene expression was reported as Phosphor Stimulating Luminescence (PSL) which reflects the level of phosphor signal generated from the probe hybridized to each of the gene targets represented on the array. A local background signal subtraction was performed before the total signal generated from each array was used to normalize gene expression between the different hybridizations. The value presented after "[array code]:" represents the mean of the duplicate values, following background subtraction and probe normalization. One of skill in the art could routinely use this information to identify normal and/or diseased tissue(s) which show a predominant expression pattern of the corresponding polynucleotide of the invention or to identify polynucleotides which show predominant and/or specific tissue and/or cell expression.

Table 1C. The polynucleotides or polypeptides, or agonists or antagonists of the present invention can be used in assays to test for one or more biological activities. If these polynucleotides and polypeptides do exhibit activity in a particular assay, it is likely that these molecules may be involved in the diseases associated with the biological activity. Thus, the polynucleotides or polypeptides, or agonists or antagonists could be used to treat the associated disease.

The present invention encompasses methods of preventing, treating, diagnosing, or ameliorating a disease or disorder. In preferred embodiments, the present invention encompasses a method of treating a disease or disorder listed in the "Preferred Indications" column of Table 1C; comprising administering to a patient in which such treatment, prevention, or amelioration is desired a protein, nucleic acid, or

antibody of the invention (or fragment or variant thereof) in an amount effective to treat, prevent, diagnose, or ameliorate the disease or disorder. The first and seccond columns of Table 1C show the "Gene No." and "cDNA Clone ID No.", respectively, indicating certain nucleic acids and proteins (or antibodies against the same) of the invention (including polynucleotide, polypeptide, and antibody fragments or variants thereof) that may be used in preventing, treating, diagnosing, or ameliorating the disease(s) or disorder(s) indicated in the corresponding row in Column 3 of Table 1C.

In another embodiment, the present invention also encompasses methods of preventing, treating, diagnosing, or ameliorating a disease or disorder listed in the "Preferred Indications" column of Table 1C; comprising administering to a patient combinations of the proteins, nucleic acids, or antibodies of the invention (or fragments or variants thereof), sharing similar indications as shown in the corresponding rows in Column 3 of Table 1C.

The “Preferred Indication” column describes diseases, disorders, and/or conditions that may be treated, prevented, diagnosed, or ameliorated by a protein, nucleic acid, or antibody of the invention (or fragment or variant thereof).

The recitation of “Cancer” in the “Preferred Indication” column indicates that the corresponding nucleic acid and protein, or antibody against the same, of the invention (or fragment or variant thereof) may be used for example, to diagnose, treat, prevent, and/or ameliorate diseases and/or disorders relating to neoplastic diseases (e.g., leukemias, cancers, and/or as described below under “Hyperproliferative Disorders”).

In specific embodiments, a protein, nucleic acid, or antibody of the invention (or fragment or variant thereof) having a “Cancer” recitation in the “Preferred Indication” column of Table 1C may be used for example, to diagnose, treat, prevent, and/or ameliorate a neoplasm located in a tissue selected from the group consisting of: colon, abdomen, bone, breast, digestive system, liver, pancreas, prostate, peritoneum, lung, blood (e.g., leukemia), endocrine glands (adrenal, parathyroid, pituitary, testicles, ovary, thymus, thyroid), uterus, eye, head and neck, nervous (central and peripheral), lymphatic system, pelvic, skin, soft tissue, spleen, thoracic, and urogenital.

In specific embodiments, a protein, nucleic acid, or antibody of the invention (or fragment or variant thereof) having a "Cancer" recitation in the "Preferred Indication" column of Table 1C, may be used for example, to diagnose, treat, prevent, and/or ameliorate a pre-neoplastic condition, selected from the group consisting of: hyperplasia (e.g., endometrial hyperplasia and/or as described in the section entitled "Hyperproliferative Disorders"), metaplasia (e.g., connective tissue metaplasia, atypical metaplasia, and/or as described in the section entitled "Hyperproliferative Disorders"), and/or dysplasia (e.g., cervical dysplasia, and bronchopulmonary dysplasia).

In another specific embodiment, a protein, nucleic acid, or antibody of the invention (or fragment or variant thereof) having a "Cancer" recitation in the "Preferred Indication" column of Table 1C, may be used for example, to diagnose, treat, prevent, and/or ameliorate a benign dysproliferative disorder selected from the group consisting of: benign tumors, fibrocystic conditions, tissue hypertrophy, and/or as described in the section entitled "Hyperproliferative Disorders".

The recitation of "Immune/Hematopoietic" in the "Preferred Indication" column indicates that the corresponding nucleic acid and protein, or antibody against the same, of the invention (or fragment or variant thereof), may be used for example, to diagnose, treat, prevent, and/or ameliorate diseases and/or disorders relating to neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Immune Activity" "Cardiovascular Disorders" and/or "Blood-Related Disorders"), and infections (e.g., as described below under "Infectious Disease").

In specific embodiments, a protein, nucleic acid, or antibody of the invention (or fragment or variant thereof) having the "Immune/Hematopoietic" recitation in the "Preferred Indication" column of Table 1C, may be used for example, to diagnose, treat, prevent, and/or ameliorate a disease or disorder selected from the group consisting of: anemia, pancytopenia, leukopenia, thrombocytopenia, leukemias, Hodgkin's disease, non-Hodgkin's lymphoma, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, asthma, AIDS, autoimmune disease, rheumatoid arthritis, granulomatous disease, immune deficiency, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, immune

reactions to transplanted organs and tissues, systemic lupus erythematosis, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and allergies.

The recitation of "Reproductive" in the "Preferred Indication" column indicates that the corresponding nucleic acid and protein, or antibody against the same, of the invention (or fragment or variant thereof), may be used for example, to diagnose, treat, prevent, and/or ameliorate diseases and/or disorders relating to neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), and disorders of the reproductive system (e.g., as described below under "Reproductive System Disorders").

In specific embodiments, a protein, nucleic acid, or antibody of the invention (or fragment or variant thereof) having a "Reproductive" recitation in the "Preferred Indication" column of Table 1C, may be used for example, to diagnose, treat, prevent, and/or ameliorate a disease or disorder selected from the group consisting of: cryptorchism, prostatitis, inguinal hernia, varicocele, leydig cell tumors, verrucous carcinoma, prostatitis, malacoplakia, Peyronie's disease, penile carcinoma, squamous cell hyperplasia, dysmenorrhea, ovarian adenocarcinoma, Turner's syndrome, mucopurulent cervicitis, Sertoli-leydig tumors, ovarian cancer, uterine cancer, pelvic inflammatory disease, testicular cancer, prostate cancer, Klinefelter's syndrome, Young's syndrome, premature ejaculation, diabetes mellitus, cystic fibrosis, Kartagener's syndrome, testicular atrophy, testicular feminization, anorchia, ectopic testis, epididymitis, orchitis, gonorrhea, syphilis, testicular torsion, vasitis nodosa, germ cell tumors, stromal tumors, dysmenorrhea, retroverted uterus, endometriosis, fibroids, adenomyosis, anovulatory bleeding, amenorrhea, Cushing's syndrome, hydatidiform moles, Asherman's syndrome, premature menopause, precocious puberty, uterine polyps, dysfunctional uterine bleeding, cervicitis, chronic cervicitis, mucopurulent cervicitis, cervical dysplasia, cervical polyps, Nabothian cysts, cervical erosion, cervical incompetence, cervical neoplasms, pseudohermaphroditism, and premenstrual syndrome.

The recitation of "Musculoskeletal" in the "Preferred Indication" column indicates that the corresponding nucleic acid and protein, or antibody against the same, of the invention (or fragment or variant thereof), may be used for example, to

diagnose, treat, prevent, and/or ameliorate diseases and/or disorders relating to neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), and disorders of the immune system (e.g., as described below under "Immune Activity").

In specific embodiments, a protein, nucleic acid, or antibody of the invention (or fragment or variant thereof) having a "Musculoskeletal" recitation in the "Preferred Indication" column of Table 1C, may be used for example, to diagnose, treat, prevent, and/or ameliorate a disease or disorder selected from the group consisting of: bone cancers (e.g., osteochondromas, benign chondromas, chondroblastoma, chondromyxoid fibromas, osteoid osteomas, giant cell tumors, multiple myeloma, osteosarcomas), Paget's Disease, rheumatoid arthritis, systemic lupus erythematosus, osteomyelitis, Lyme Disease, gout, bursitis, tendonitis, osteoporosis, osteoarthritis, muscular dystrophy, mitochondrial myopathy, cachexia, and multiple sclerosis.

The recitation of "Cardiovascular" in the "Preferred Indication" column indicates that the corresponding nucleic acid and protein, or antibody against the same, of the invention (or fragment or variant thereof), may be used for example, to diagnose, treat, prevent, and/or ameliorate diseases and/or disorders relating to neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), and disorders of the cardiovascular system (e.g., as described below under "Cardiovascular Disorders").

In specific embodiments, a protein, nucleic acid, or antibody of the invention (or fragment or variant thereof) having a "Cardiovascular" recitation in the "Preferred Indication" column of Table 1C, may be used for example, to diagnose, treat, prevent, and/or ameliorate a disease or disorder selected from the group consisting of: myxomas, fibromas, rhabdomyomas, cardiovascular abnormalities (e.g., congenital heart defects, cerebral arteriovenous malformations, septal defects), heart disease (e.g., heart failure, congestive heart disease, arrhythmia, tachycardia, fibrillation, pericardial Disease, endocarditis), cardiac arrest, heart valve disease (e.g., stenosis, regurgitation, prolapse), vascular disease (e.g., hypertension, coronary artery disease, angina, aneurysm, arteriosclerosis, peripheral vascular disease), hyponatremia, hypernatremia, hypokalemia, and hyperkalemia.

The recitation of "Mixed Fetal" in the "Preferred Indication" column indicates that the corresponding nucleic acid and protein, or antibody against the same, of the invention (or fragment or variant thereof), may be used for example, to diagnose, treat, prevent, and/or ameliorate diseases and/or disorders relating to neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders").

In specific embodiments, a protein, nucleic acid, or antibody of the invention (or fragment or variant thereof) having a "Mixed Fetal" recitation in the "Preferred Indication" column of Table 1C, may be used for example, to diagnose, treat, prevent, and/or ameliorate a disease or disorder selected from the group consisting of: spina bifida, hydranencephaly, neurofibromatosis, fetal alcohol syndrome, diabetes mellitus, PKU, Down's syndrome, Patau syndrome, Edwards syndrome, Turner syndrome, Apert syndrome, Carpenter syndrome, Conradi syndrome, Crouzon syndrome, cutis laxa, Cornelia de Lange syndrome, Ellis-van Creveld syndrome, Holt-Oram syndrome, Kartagener syndrome, Meckel-Gruber syndrome, Noonan syndrome, Pallister-Hall syndrome, Rubinstein-Taybi syndrome, Scimitar syndrome, Smith-Lemli-Opitz syndrome, thromocytopenia-absent radius (TAR) syndrome, Treacher Collins syndrome, Williams syndrome, Hirschsprung's disease, Meckel's diverticulum, polycystic kidney disease, Turner's syndrome, and gonadal dysgenesis, Klippel-Feil syndrome, Ostogenesis imperfecta, muscular dystrophy, Tay-Sachs disease, Wilm's tumor, neuroblastoma, and retinoblastoma.

The recitation of "Excretory" in the "Preferred Indication" column indicates that the corresponding nucleic acid and protein, or antibody against the same, of the invention (or fragment or variant thereof), may be used for example, to diagnose, treat, prevent, and/or ameliorate diseases and/or disorders relating to neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders") and renal disorders (e.g., as described below under "Renal Disorders").

In specific embodiments, a protein, nucleic acid, or antibody of the invention (or fragment or variant thereof) having a "Excretory" recitation in the "Preferred Indication" column of Table 1C, may be used for example, to diagnose, treat, prevent, and/or ameliorate a disease or disorder selected from the group consisting of: bladder cancer, prostate cancer, benign prostatic hyperplasia, bladder disorders (e.g., urinary incontinence, urinary retention, urinary obstruction, urinary tract Infections,

interstitial cystitis, prostatitis, neurogenic bladder, hematuria), renal disorders (e.g., hydronephrosis, proteinuria, renal failure, pyelonephritis, urolithiasis, reflux nephropathy, and unilateral obstructive uropathy).

The recitation of "Neural/Sensory" in the "Preferred Indication" column indicates that the corresponding nucleic acid and protein, or antibody against the same, of the invention (or fragment or variant thereof), may be used for example, to diagnose, treat, prevent, and/or ameliorate diseases and/or disorders relating to neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders") and diseases or disorders of the nervous system (e.g., as described below under "Neural Activity and Neurological Diseases").

In specific embodiments, a protein, nucleic acid, or antibody of the invention (or fragment or variant thereof) having a "Neural/Sensory" recitation in the "Preferred Indication" column of Table 1C, may be used for example, to diagnose, treat, prevent, and/or ameliorate a disease or disorder selected from the group consisting of: brain cancer (e.g., brain stem glioma, brain tumors, central nervous system (Primary) lymphoma, central nervous system lymphoma, cerebellar astrocytoma, and cerebral astrocytoma, neurodegenerative disorders (e.g., Alzheimer's Disease, Creutzfeldt-Jakob Disease, Parkinson's Disease, and Idiopathic Presenile Dementia), encephalomyelitis, cerebral malaria, meningitis, metabolic brain diseases (e.g., phenylketonuria and pyruvate carboxylase deficiency), cerebellar ataxia, ataxia telangiectasia, and AIDS Dementia Complex, schizophrenia, attention deficit disorder, hyperactive attention deficit disorder, autism, and obsessive compulsive disorders.

The recitation of "Respiratory" in the "Preferred Indication" column indicates that the corresponding nucleic acid and protein, or antibody against the same, of the invention (or fragment or variant thereof), may be used for example, to diagnose, treat, prevent, and/or ameliorate diseases and/or disorders relating to neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders") and diseases or disorders of the respiratory system (e.g., as described below under "Respiratory Disorders").

In specific embodiments, a protein, nucleic acid, or antibody of the invention (or fragment or variant thereof) having a "Respiratory" recitation in the "Preferred

Indication" column of Table 1C, may be used for example, to diagnose, treat, prevent, and/or ameliorate a disease or disorder selected from the group consisting of: cancers of the respiratory system such as larynx cancer, pharynx cancer, trachea cancer, epiglottis cancer, lung cancer, squamous cell carcinomas, small cell (oat cell) carcinomas, large cell carcinomas, and adenocarcinomas. Allergic reactions, cystic fibrosis, sarcoidosis, histiocytosis X, infiltrative lung diseases (e.g., pulmonary fibrosis and lymphoid interstitial pneumonia), obstructive airway diseases (e.g., asthma, emphysema, chronic or acute bronchitis), occupational lung diseases (e.g., silicosis and asbestosis), pneumonia, and pleurisy.

The recitation of "Endocrine" in the "Preferred Indication" column indicates that the corresponding nucleic acid and protein, or antibody against the same, of the invention (or fragment or variant thereof), may be used for example, to diagnose, treat, prevent, and/or ameliorate diseases and/or disorders relating to neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders") and diseases or disorders of the respiratory system (e.g., as described below under "Respiratory Disorders"), renal disorders (e.g., as described below under "Renal Disorders"), and disorders of the endocrine system (e.g., as described below under "Endocrine Disorders".

In specific embodiments, a protein, nucleic acid, or antibody of the invention (or fragment or variant thereof) having an "Endocrine" recitation in the "Preferred Indication" column of Table 1C, may be used for example, to diagnose, treat, prevent, and/or ameliorate a disease or disorder selected from the group consisting of: cancers of endocrine tissues and organs (e.g., cancers of the hypothalamus, pituitary gland, thyroid gland, parathyroid glands, pancreas, adrenal glands, ovaries, and testes), diabetes (e.g., diabetes insipidus, type I and type II diabetes mellitus), obesity, disorders related to pituitary glands (e.g., hyperpituitarism, hypopituitarism, and pituitary dwarfism), hypothyroidism, hyperthyroidism, goiter, reproductive disorders (e.g. male and female infertility), disorders related to adrenal glands (e.g., Addison's Disease, corticosteroid deficiency, and Cushing's Syndrome), kidney cancer (e.g., hypernephroma, transitional cell cancer, and Wilm's tumor), diabetic nephropathy, interstitial nephritis, polycystic kidney disease, glomerulonephritis (e.g., IgM

mesangial proliferative glomerulonephritis and glomerulonephritis caused by autoimmune disorders; such as Goodpasture's syndrome), and nephrocalcinosis.

The recitation of "Digestive" in the "Preferred Indication" column indicates that the corresponding nucleic acid and protein, or antibody against the same, of the invention (or fragment or variant thereof), may be used for example, to diagnose, treat, prevent, and/or ameliorate diseases and/or disorders relating to neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders") and diseases or disorders of the gastrointestinal system (e.g., as described below under "Gastrointestinal Disorders".

In specific embodiments, a protein, nucleic acid, or antibody of the invention (or fragment or variant thereof) having a "Digestive" recitation in the "Preferred Indication" column of Table 1C, may be used for example, to diagnose, treat, prevent, and/or ameliorate a disease or disorder selected from the group consisting of: ulcerative colitis, appendicitis, Crohn's disease, hepatitis, hepatic encephalopathy, portal hypertension, cholelithiasis, cancer of the digestive system (e.g., biliary tract cancer, stomach cancer, colon cancer, gastric cancer, pancreatic cancer, cancer of the bile duct, tumors of the colon (e.g., polyps or cancers), and cirrhosis), pancreatitis, ulcerative disease, pyloric stenosis, gastroenteritis, gastritis, gastric atropy, benign tumors of the duodenum, distension, irritable bowel syndrome, malabsorption, congenital disorders of the small intestine, bacterial and parasitic infection, megacolon, Hirschsprung's disease, aganglionic megacolon, acquired megacolon, colitis, anorectal disorders (e.g., anal fistulas, hemorrhoids), congenital disorders of the liver (e.g., Wilson's disease, hemochromatosis, cystic fibrosis, biliary atresia, and alpha1-antitrypsin deficiency), portal hypertension, cholelithiasis, and jaundice.

The recitation of "Connective/Epithelial" in the "Preferred Indication" column indicates that the corresponding nucleic acid and protein, or antibody against the same, of the invention (or fragment or variant thereof), may be used for example, to diagnose, treat, prevent, and/or ameliorate diseases and/or disorders relating to neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), cellular and genetic abnormalities (e.g., as described below under "Diseases at the Cellular Level "), angiogenesis (e.g., as described below under "Anti-Angiogenesis Activity "), and or to promote or inhibit regeneration (e.g., as described below under

"Regeneration "), and wound healing (e.g., as described below under "Wound Healing and Epithelial Cell Proliferation").

In specific embodiments, a protein, nucleic acid, or antibody of the invention (or fragment or variant thereof) having a "Connective/Epithelial" recitation in the "Preferred Indication" column of Table 1C, may be used for example, to diagnose, treat, prevent, and/or ameliorate a disease or disorder selected from the group consisting of: connective tissue metaplasia, mixed connective tissue disease, focal epithelial hyperplasia, epithelial metaplasia, mucoepithelial dysplasia, graft v. host disease, polymyositis, cystic hyperplasia, cerebral dysplasia, tissue hypertrophy, Alzheimer's disease, lymphoproliferative disorder, Waldenstron's macroglobulinemia, Crohn's disease, pernicious anemia, idiopathic Addison's disease, glomerulonephritis, bullous pemphigoid, Sjogren's syndrome, diabetes mellitus, cystic fibrosis, osteoblastoma, osteoclastoma, osteosarcoma, chondrosarcoma, osteoporosis, osteocarthritis, periodontal disease, wound healing, relapsing polychondritis, vasculitis, polyarteritis nodosa, Wegener's granulomatosis, cellulitis, rheumatoid arthritis, psoriatic arthritis, discoid lupus erythematosus, systemic lupus erythematosus, scleroderma, CREST syndrome, Sjogren's syndrome, polymyositis, dermatomyositis, mixed connective tissue disease, relapsing polychondritis, vasculitis, Henoch-Schonlein syndrome, erythema nodosum, polyarteritis nodosa, temporal (giant cell) arteritis, Takayasu's arteritis, Wegener's granulomatosis, Reiter's syndrome, Behcet's syndrome, ankylosing spondylitis, cellulitis, keloids, Ehler Danlos syndrome, Marfan syndrome, pseudoxantoma elasticum, osteogenese imperfecta, chondrodysplasias, epidermolysis bullosa, Alport syndrome, and cutis laxa.

Moreover, polynucleotides, translation products and antibodies corresponding to this gene may be useful for the diagnosis, prognosis, prevention, and/or treatment of diseases and/or disorders associated with the following systems.

Table 2 summarizes homology and features of some of the polypeptides of the invention. The first column provides a unique clone identifier, "Clone ID NO", corresponding to a cDNA clone disclosed in Table 1A or 1B. The second column provides the unique contig identifier, "Contig ID:" corresponding to contigs in Table 1B and allowing for correlation with the information in Table 1B. The third column

provides the sequence identifier, "SEQ ID NO:X", for the contig polynucleotide sequence. The fourth column provides the analysis method by which the homology/identity disclosed in the Table was determined. Comparisons were made between polypeptides encoded by the polynucleotides of the invention and either a non-redundant protein database (herein referred to as "NR"), or a database of protein families (herein referred to as "PFAM") as further described below. The fifth column provides a description of the PFAM/NR hit having a significant match to a polypeptide of the invention. Column six provides the accession number of the PFAM/NR hit disclosed in the fifth column. Column seven, "Score/Percent Identity", provides a quality score or the percent identity, of the hit disclosed in columns five and six. Columns 8 and 9, "NT From" and "NT To" respectively, delineate the polynucleotides in "SEQ ID NO:X" that encode a polypeptide having a significant match to the PFAM/NR database as disclosed in the fifth and sixth columns. In specific embodiments polypeptides of the invention comprise, or alternatively consist of, an amino acid sequence encoded by a polynucleotide in SEQ ID NO:X as delineated in columns 8 and 9, or fragments or variants thereof.

Table 3 provides polynucleotide sequences that may be disclaimed according to certain embodiments of the invention. The first column provides a unique clone identifier, "Clone ID NO", for a cDNA clone related to contig sequences disclosed in Table 1B. The second column provides the sequence identifier, "SEQ ID NO:X", for contig sequences disclosed in Table 1A and/or 1B. The third column provides the unique contig identifier, "Contig ID:", for contigs disclosed in Table 1B. The fourth column provides a unique integer 'a' where 'a' is any integer between 1 and the final nucleotide minus 15 of SEQ ID NO:X, and the fifth column provides a unique integer 'b' where 'b' is any integer between 15 and the final nucleotide of SEQ ID NO:X, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:X, and where b is greater than or equal to a + 14. For each of the polynucleotides shown as SEQ ID NO:X, the uniquely defined integers can be substituted into the general formula of a-b, and used to describe polynucleotides which may be preferably excluded from the invention. In certain embodiments, preferably excluded from the invention are at least one, two, three, four, five, ten, or more of the polynucleotide sequence(s) having the accession number(s) disclosed in

the sixth column of this Table (including for example, published sequence in connection with a particular BAC clone). In further embodiments, preferably excluded from the invention are the specific polynucleotide sequence(s) contained in the clones corresponding to at least one, two, three, four, five, ten, or more of the available material having the accession numbers identified in the sixth column of this Table (including for example, the actual sequence contained in an identified BAC clone).

Table 4 provides a key to the tissue/cell source identifier code disclosed in Table 1B, column 8. Column 1 provides the tissue/cell source identifier code disclosed in Table 1B, Column 8. Columns 2-5 provide a description of the tissue or cell source. Codes corresponding to diseased tissues are indicated in column 6 with the word "disease". The use of the word "disease" in column 6 is non-limiting. The tissue or cell source may be specific (e.g. a neoplasm), or may be disease-associated (e.g., a tissue sample from a normal portion of a diseased organ). Furthermore, tissues and/or cells lacking the "disease" designation may still be derived from sources directly or indirectly involved in a disease state or disorder, and therefore may have a further utility in that disease state or disorder. In numerous cases where the tissue/cell source is a library, column 7 identifies the vector used to generate the library.

Table 5, column 1, provides a nucleotide sequence identifier, "SEQ ID NO:X," that matches a nucleotide SEQ ID NO:X disclosed in Table 1A, column 5. Table 5, column 2, provides the chromosomal location, "Cytologic Band or Chromosome," of polynucleotides corresponding to SEQ ID NO:X. Chromosomal location was determined by finding exact matches to EST and cDNA sequences contained in the NCBI (National Center for Biotechnology Information) UniGene database. Given a presumptive chromosomal location, disease locus association was determined by comparison with the Morbid Map, derived from Online Mendelian Inheritance in Man (Online Mendelian Inheritance in Man, OMIM™. McKusick-Nathans Institute for Genetic Medicine, Johns Hopkins University (Baltimore, MD) and National Center for Biotechnology Information, National Library of Medicine (Bethesda, MD) 2000. World Wide Web URL: http://www.ncbi.nlm.nih.gov/omim/). If the putative chromosomal location of the Query overlapped with the chromosomal

location of a Morbid Map entry, the OMIM reference identification number of the morbid map entry is provided in Table 5, column 3, labelled "OMIM Reference(s)." A key to the OMIM reference identification numbers is provided in Table 6.

Table 6 provides a key to the OMIM reference identification numbers disclosed in Table 5, column 3. OMIM reference identification numbers (Column 1) were derived from Online Mendelian Inheritance in Man (Online Mendelian Inheritance in Man, OMIM. McKusick-Nathans Institute for Genetic Medicine, Johns Hopkins University (Baltimore, MD) and National Center for Biotechnology Information, National Library of Medicine, (Bethesda, MD) 2000. World Wide Web URL: http://www.ncbi.nlm.nih.gov/omim/). Column 2 provides diseases associated with the cytologic band disclosed in Table 5, column 2, as determined using the Morbid Map database.

Definitions

The following definitions are provided to facilitate understanding of certain terms used throughout this specification.

In the present invention, "isolated" refers to material removed from its original environment (e.g., the natural environment if it is naturally occurring), and thus is altered "by the hand of man" from its natural state. For example, an isolated polynucleotide could be part of a vector or a composition of matter, or could be contained within a cell, and still be "isolated" because that vector, composition of matter, or particular cell is not the original environment of the polynucleotide. The term "isolated" does not refer to genomic or cDNA libraries, whole cell total or mRNA preparations, genomic DNA preparations (including those separated by electrophoresis and transferred onto blots), sheared whole cell genomic DNA preparations or other compositions where the art demonstrates no distinguishing features of the polynucleotide/sequences of the present invention.

In the present invention, a "secreted" protein refers to those proteins capable of being directed to the ER, secretory vesicles, or the extracellular space as a result of a signal sequence, as well as those proteins released into the extracellular space without necessarily containing a signal sequence. If the secreted protein is released

into the extracellular space, the secreted protein can undergo extracellular processing to produce a "mature" protein. Release into the extracellular space can occur by many mechanisms, including exocytosis and proteolytic cleavage.

As used herein, a "polynucleotide" refers to a molecule having a nucleic acid sequence contained in SEQ ID NO:X (as described in column 5 of Table 1A), or cDNA clone (as described in column 2 of Table 1A and contained within a pool of plasmids deposited with the ATCC in ATCC Deposit No:Z). For example, the polynucleotide can contain the nucleotide sequence of the full length cDNA sequence, including the 5' and 3' untranslated sequences, the coding region, with or without a natural or artificial signal sequence, the protein coding region, as well as fragments, epitopes, domains, and variants of the nucleic acid sequence. Moreover, as used herein, a "polypeptide" refers to a molecule having an amino acid sequence encoded by a polynucleotide of the invention as broadly defined (obviously excluding poly-Phenylalanine or poly-Lysine peptide sequences which result from translation of a polyA tail of a sequence corresponding to a cDNA).

In the present invention, a representative plasmid containing the sequence of SEQ ID NO:X was deposited with the American Type Culture Collection ("ATCC") and/or described in Table 1A. As shown in Table 1A, each cDNA is identified by a cDNA clone identifier and the ATCC Deposit Number (ATCC Deposit No:Z). Plasmids that were pooled and deposited as a single deposit have the same ATCC Deposit Number. The ATCC is located at 10801 University Boulevard, Manassas, Virginia 20110-2209, USA. The ATCC deposit was made pursuant to the terms of the Budapest Treaty on the international recognition of the deposit of microorganisms for purposes of patent procedure.

A "polynucleotide" of the present invention also includes those polynucleotides capable of hybridizing, under stringent hybridization conditions, to sequences contained in SEQ ID NO:X, or the complement thereof (e.g., the complement of any one, two, three, four, or more of the polynucleotide fragments described herein) and/or sequences of the cDNA contained in the deposited clone (e.g., the complement of any one, two, three, four, or more of the polynucleotide fragments described herein). "Stringent hybridization conditions" refers to an overnight incubation at 42 degree C in a solution comprising 50% formamide, 5x SSC

(750 mM NaCl, 75 mM trisodium citrate), 50 mM sodium phosphate (pH 7.6), 5x Denhardt's solution, 10% dextran sulfate, and 20 μg/ml denatured, sheared salmon sperm DNA, followed by washing the filters in 0.1x SSC at about 65 degree C.

Also included within "polynucleotides" of the present invention are nucleic acid molecules that hybridize to the polynucleotides of the present invention at lower stringency hybridization conditions. Changes in the stringency of hybridization and signal detection are primarily accomplished through the manipulation of formamide concentration (lower percentages of formamide result in lowered stringency); salt conditions, or temperature. For example, lower stringency conditions include an overnight incubation at 37 degree C in a solution comprising 6X SSPE (20X SSPE = 3M NaCl; 0.2M NaH_2PO_4; 0.02M EDTA, pH 7.4), 0.5% SDS, 30% formamide, 100 μg/ml salmon sperm blocking DNA; followed by washes at 50 degree C with 1XSSPE, 0.1% SDS. In addition, to achieve even lower stringency, washes performed following stringent hybridization can be done at higher salt concentrations (e.g. 5X SSC).

Note that variations in the above conditions may be accomplished through the inclusion and/or substitution of alternate blocking reagents used to suppress background in hybridization experiments. Typical blocking reagents include Denhardt's reagent, BLOTTO, heparin, denatured salmon sperm DNA, and commercially available proprietary formulations. The inclusion of specific blocking reagents may require modification of the hybridization conditions described above, due to problems with compatibility.

Of course, a polynucleotide which hybridizes only to polyA+ sequences (such as any 3' terminal polyA+ tract of a cDNA shown in the sequence listing), or to a complementary stretch of T (or U) residues, would not be included in the definition of "polynucleotide," since such a polynucleotide would hybridize to any nucleic acid molecule containing a poly (A) stretch or the complement thereof (e.g., practically any double-stranded cDNA clone generated using oligo dT as a primer).

The polynucleotides of the present invention can be composed of any polyribonucleotide or polydeoxribonucleotide, which may be unmodified RNA or DNA or modified RNA or DNA. For example, polynucleotides can be composed of single- and double-stranded DNA, DNA that is a mixture of single- and double-

stranded regions, single- and double-stranded RNA, and RNA that is mixture of single- and double-stranded regions, hybrid molecules comprising DNA and RNA that may be single-stranded or, more typically, double-stranded or a mixture of single- and double-stranded regions. In addition, the polynucleotide can be composed of triple-stranded regions comprising RNA or DNA or both RNA and DNA. A polynucleotide may also contain one or more modified bases or DNA or RNA backbones modified for stability or for other reasons. "Modified" bases include, for example, tritylated bases and unusual bases such as inosine. A variety of modifications can be made to DNA and RNA; thus, "polynucleotide" embraces chemically, enzymatically, or metabolically modified forms.

In specific embodiments, the polynucleotides of the invention are at least 15, at least 30, at least 50, at least 100, at least 125, at least 500, or at least 1000 continuous nucleotides but are less than or equal to 300 kb, 200 kb, 100 kb, 50 kb, 15 kb, 10 kb, 7.5kb, 5 kb, 2.5 kb, 2.0 kb, or 1 kb, in length. In a further embodiment, polynucleotides of the invention comprise a portion of the coding sequences, as disclosed herein, but do not comprise all or a portion of any intron. In another embodiment, the polynucleotides comprising coding sequences do not contain coding sequences of a genomic flanking gene (i.e., 5' or 3' to the gene of interest in the genome). In other embodiments, the polynucleotides of the invention do not contain the coding sequence of more than 1000, 500, 250, 100, 50, 25, 20, 15, 10, 5, 4, 3, 2, or 1 genomic flanking gene(s).

"SEQ ID NO:X" refers to a polynucleotide sequence described in column 5 of Table 1A, while "SEQ ID NO:Y" refers to a polypeptide sequence described in column 10 of Table 1A. SEQ ID NO:X is identified by an integer specified in column 6 of Table 1A. The polypeptide sequence SEQ ID NO:Y is a translated open reading frame (ORF) encoded by polynucleotide SEQ ID NO:X. The polynucleotide sequences are shown in the sequence listing immediately followed by all of the polypeptide sequences. Thus, a polypeptide sequence corresponding to polynucleotide sequence SEQ ID NO:2 is the first polypeptide sequence shown in the sequence listing. The second polypeptide sequence corresponds to the polynucleotide sequence shown as SEQ ID NO:3, and so on.

The polypeptides of the present invention can be composed of amino acids joined to each other by peptide bonds or modified peptide bonds, i.e., peptide isosteres, and may contain amino acids other than the 20 gene-encoded amino acids. The polypeptides may be modified by either natural processes, such as posttranslational processing, or by chemical modification techniques which are well known in the art. Such modifications are well described in basic texts and in more detailed monographs, as well as in a voluminous research literature. Modifications can occur anywhere in a polypeptide, including the peptide backbone, the amino acid side-chains and the amino or carboxyl termini. It will be appreciated that the same type of modification may be present in the same or varying degrees at several sites in a given polypeptide. Also, a given polypeptide may contain many types of modifications. Polypeptides may be branched, for example, as a result of ubiquitination, and they may be cyclic, with or without branching. Cyclic, branched, and branched cyclic polypeptides may result from posttranslation natural processes or may be made by synthetic methods. Modifications include acetylation, acylation, ADP-ribosylation, amidation, covalent attachment of flavin, covalent attachment of a heme moiety, covalent attachment of a nucleotide or nucleotide derivative, covalent attachment of a lipid or lipid derivative, covalent attachment of phosphotidylinositol, cross-linking, cyclization, disulfide bond formation, demethylation, formation of covalent cross-links, formation of cysteine, formation of pyroglutamate, formylation, gamma-carboxylation, glycosylation, GPI anchor formation, hydroxylation, iodination, methylation, myristoylation, oxidation, pegylation, proteolytic processing, phosphorylation, prenylation, racemization, selenoylation, sulfation, transfer-RNA mediated addition of amino acids to proteins such as arginylation, and ubiquitination. (See, for instance, PROTEINS - STRUCTURE AND MOLECULAR PROPERTIES, 2nd Ed., T. E. Creighton, W. H. Freeman and Company, New York (1993); POSTTRANSLATIONAL COVALENT MODIFICATION OF PROTEINS, B. C. Johnson, Ed., Academic Press, New York, pgs. 1-12 (1983); Seifter et al., Meth Enzymol 182:626-646 (1990); Rattan et al., Ann NY Acad Sci 663:48-62 (1992)).

The polypeptides of the invention can be prepared in any suitable manner. Such polypeptides include isolated naturally occurring polypeptides, recombinantly produced polypeptides, synthetically produced polypeptides, or polypeptides

produced by a combination of these methods. Means for preparing such polypeptides are well understood in the art.

The polypeptides may be in the form of the secreted protein, including the mature form, or may be a part of a larger protein, such as a fusion protein (see below). It is often advantageous to include an additional amino acid sequence which contains secretory or leader sequences, pro-sequences, sequences which aid in purification, such as multiple histidine residues, or an additional sequence for stability during recombinant production.

The polypeptides of the present invention are preferably provided in an isolated form, and preferably are substantially purified. A recombinantly produced version of a polypeptide, including the secreted polypeptide, can be substantially purified using techniques described herein or otherwise known in the art, such as, for example, by the one-step method described in Smith and Johnson, Gene 67:31-40 (1988). Polypeptides of the invention also can be purified from natural, synthetic or recombinant sources using techniques described herein or otherwise known in the art, such as, for example, antibodies of the invention raised against the polypeptides of the present invention in methods which are well known in the art.

By a polypeptide demonstrating a "functional activity" is meant, a polypeptide capable of displaying one or more known functional activities associated with a full-length (complete) protein of the invention. Such functional activities include, but are not limited to, biological activity, antigenicity [ability to bind (or compete with a polypeptide for binding) to an anti-polypeptide antibody], immunogenicity (ability to generate antibody which binds to a specific polypeptide of the invention), ability to form multimers with polypeptides of the invention, and ability to bind to a receptor or ligand for a polypeptide.

"A polypeptide having functional activity" refers to polypeptides exhibiting activity similar, but not necessarily identical to, an activity of a polypeptide of the present invention, including mature forms, as measured in a particular assay, such as, for example, a biological assay, with or without dose dependency. In the case where dose dependency does exist, it need not be identical to that of the polypeptide, but rather substantially similar to the dose-dependence in a given activity as compared to the polypeptide of the present invention (i.e., the candidate polypeptide will exhibit

greater activity or not more than about 25-fold less and, preferably, not more than about tenfold less activity, and most preferably, not more than about three-fold less activity relative to the polypeptide of the present invention).

The functional activity of the polypeptides, and fragments, variants derivatives, and analogs thereof, can be assayed by various methods.

For example, in one embodiment where one is assaying for the ability to bind or compete with full-length polypeptide of the present invention for binding to an antibody to the full length polypeptide, various immunoassays known in the art can be used, including but not limited to, competitive and non-competitive assay systems using techniques such as radioimmunoassays, ELISA (enzyme linked immunosorbent assay), "sandwich" immunoassays, immunoradiometric assays, gel diffusion precipitation reactions, immunodiffusion assays, in situ immunoassays (using colloidal gold, enzyme or radioisotope labels, for example), western blots, precipitation reactions, agglutination assays (e.g., gel agglutination assays, hemagglutination assays), complement fixation assays, immunofluorescence assays, protein A assays, and immunoelectrophoresis assays, etc. In one embodiment, antibody binding is detected by detecting a label on the primary antibody. In another embodiment, the primary antibody is detected by detecting binding of a secondary antibody or reagent to the primary antibody. In a further embodiment, the secondary antibody is labeled. Many means are known in the art for detecting binding in an immunoassay and are within the scope of the present invention.

In another embodiment, where a ligand is identified, or the ability of a polypeptide fragment, variant or derivative of the invention to multimerize is being evaluated, binding can be assayed, e.g., by means well-known in the art, such as, for example, reducing and non-reducing gel chromatography, protein affinity chromatography, and affinity blotting. See generally, Phizicky, E., et al., Microbiol. Rev. 59:94-123 (1995). In another embodiment, physiological correlates polypeptide of the present invention binding to its substrates (signal transduction) can be assayed.

In addition, assays described herein (see Examples) and otherwise known in the art may routinely be applied to measure the ability of polypeptides of the present invention and fragments, variants derivatives and analogs thereof to elicit polypeptide

related biological activity (either in vitro or in vivo). Other methods will be known to the skilled artisan and are within the scope of the invention.

Polynucleotides and Polypeptides of the Invention

FEATURES OF PROTEIN ENCODED BY GENE NO: 1

The DNA in this clone is identical to a fragment of a ~2Mbp region of human DNA sequence from cosmid L98A6, Huntington's Disease Region, chromosome 4p16.3.

This gene is expressed in the following tissues/cDNA libraries: Human Amygdala; KMH2; Spleen, Chronic lymphocytic leukemia.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include but are not limited to: leukemia and other cancers. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

This clone encodes a novel secreted protein expressed in several tissues including chronic lymphocytic leukemia. The protein represents a novel therapeutic or target for the above indicated diseases. For example this protein may be a novel cytokine and thus may serve as a therapeutic or target for development of a therapeutic for diseases of the immune system such as allergy, asthma, leukemias, inflammatory diseases, and immune deficiencies. Since this DNA maps to a region associated with Huntington's disease and is expressed in amygdala, this protein may be therapuetic (or a target) for neurological disorders including Huntington's chorea.

FEATURES OF PROTEIN ENCODED BY GENE NO: 2

The computer algorithm BLASTX has been used to determine that the translation product of this gene shares sequence homology with, as a non-limiting example, the sequence accessible through the following database accession no. sp|Q93075|Y218_HUMAN (all information available through the recited accession number is incorporated herein by reference). Based on the structural similarity these homologous polypeptides are expected to share at least some biological activities. Such activities are known in the art, some of which are described elsewhere herein. Assays for determining such activities are also known in the art, some of which have been described elsewhere herein. Preferred polypeptides of the invention comprise a polypeptide having the amino acid sequence set out in the sequence listing as SEQ ID NO: 385.

This gene is expressed in the following tissues/cDNA libraries: NCI_CGAP_Pr28 and to a lesser extent in Soares adult brain N2b4HB55Y; normalized infant brain cDNA; Nine Week Old Early Stage Human; NCI_CGAP_Kid12; NCI_CGAP_Co16; NCI_CGAP_Kid8; NCI_CGAP_Lu24; Human Adult Skeletal Muscle; Stromal cells 3.88; human corpus colosum; B Cell lymphoma; Soares breast 2NbHBst; Smooth muscle, serum induced,re-exc; Smooth muscle, serum treated; NCI_CGAP_Kid11; NCI_CGAP_GC6; T Cell helper I; Human 8 Week Whole Embryo and Soares fetal liver spleen 1NFLS.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of neurological disorders; particularly brain cancer and neurodegenerative disorders (such as Alzheimer's, Parkinson's and Huntington's Disease). See "Neural Activity and Neurological Diseases" section, infra. The tissue distribution also indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of cancer and other hyperproliferative disorders (e.g., see "Hyperproliferative Disorders" section, infra).

FEATURES OF PROTEIN ENCODED BY GENE NO: 3

This gene is expressed in Human Thymus Stromal Cells.

Polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of cancer and other proliferative disorders as well as type II diabetes. Accordingly, polynucleotides and/or polypeptides of the invention and/or antagonists thereof (especially neutralizing or antagonistic antibodies) may be used to treat, prevent, and/or ameliorate type II diabetes. Additionally, in other embodiments, the polynucleotides and/or polypeptides corresponding to this gene and/or antagonists thereof (especially neutralizing or antagonistic antibodies) may be used to treat, prevent, or ameliorate conditions associated with type II diabetes mellitus, including, but not limited to, seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, kidney disease (e.g., renal failure, nephropathy other diseases and disorders as described in the "Renal Disorders" section below), endocrine disorders (as described in the "Endocrine Disorders" section below), obesity, nerve damage, neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, infections (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture. In another embodiment, the polynucleotides and/or polypeptides of the invention and/or antagonists thereof (especially neutralizing or antagonistic antibodies) may be used to treat, prevent, and/or ameliorate diabetes and/or complication associated with diabetes. Complications associated with diabetes include: blindness (e.g., due to diabetic retinopathy), kidney disease (e.g., due to diabetic nephropathy), nerve disease (e.g., due to diabetic neuropathy) and amputations, heart disease and stroke, and impotence (e.g., due to diabetic neuropathy or blood vessel blockage. In additional preferred embodiments, polypeptides, polynucleotides, antibodies, agonists, or antagonists corresponding to that polypeptide, may be used to regulate weight gain, weight loss, and/or obesity. In other embodiments, the polynucleotides and/or polypeptides of the

invention and/or antagonists thereof (especially neutralizing or antagonistic antibodies) may be used to treat, prevent, and/or ameliorate other diseases or disorders described herein (See, e.g.,. "Biological Activities" section and the sections cross-referenced therein).

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of immune system disorders; particularly immune cell proliferative disorders (e.g. leukemia), autoimmune disorders, and immunodeficiencies (including immunodeficiencies caused by genetic factors, microbial pathogens (e.g. HIV), chemotherapy, and radiation). See "Immune Activity" section, infra.

FEATURES OF PROTEIN ENCODED BY GENE NO: 4

This gene is expressed in the following tissues/cDNA libraries: Human Neutrophil, Activated; Human Neutrophils, Activated, re-excision; Human Eosinophils and to a lesser extent in Human Neutrophil; Human Fetal Heart.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of immune system disorders; particularly immune cell proliferative disorders (e.g. leukemia), autoimmune disorders, and immunodeficiencies (including immunodeficiencies caused by genetic factors, microbial pathogens (e.g. HIV), chemotherapy, and radiation). See "Immune Activity" section, infra.

FEATURES OF PROTEIN ENCODED BY GENE NO: 5

The computer algorithm BLASTX has been used to determine that the translation product of this gene shares sequence homology with, as a non-limiting example, the sequence accessible through the following database accession no. pir|D82426|D82426 (all information available through the recited accession number is incorporated herein by reference). Based on the structural similarity these homologous polypeptides are expected to share at least some biological activities. Such activities are known in the art, some of which are described elsewhere herein.

Assays for determining such activities are also known in the art, some of which have been described elsewhere herein. Preferred polypeptides of the invention comprise a polypeptide having the amino acid sequence set out in the sequence listing as SEQ ID NO:386 .

This gene is expressed in the following tissues/cDNA libraries: Soares_fetal_liver_spleen_1NFLS_S1 and to a lesser extent in H. Frontal cortex,epileptic,re-excision; stromal cell clone 2.5; Human Primary Breast Cancer; NCI_CGAP_Ut4; NCI_CGAP_Ut2; Hemangiopericytoma; NCI_CGAP_CLL1; NCI_CGAP_Brn25; T-Cell PHA 24 hrs; Soares_fetal_lung_NbHL19W and Soares_NFL_T_GBC_S1.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of cancer and other hyperproliferative disorders (e.g., see "Hyperproliferative Disorders" section, infra).

FEATURES OF PROTEIN ENCODED BY GENE NO: 6

The computer algorithm BLASTX has been used to determine that the translation product of this gene shares sequence homology with, as a non-limiting example, the sequence accessible through the following database accession no. pir|S27956|S27956 (all information available through the recited accession number is incorporated herein by reference). Based on the structural similarity these homologous polypeptides are expected to share at least some biological activities. Such activities are known in the art, some of which are described elsewhere herein. Assays for determining such activities are also known in the art, some of which have been described elsewhere herein. Preferred polypeptides of the invention comprise a polypeptide having the amino acid sequence set out in the sequence listing as SEQ ID NO:387.

This gene is expressed in the following tissues/cDNA libraries: Soares retina N2b4HR and to a lesser extent in stromal cell clone 2.5; Human Quadriceps; NCI_CGAP_Pr28; Human Testes, Reexcision; NCI_CGAP_Kid3 and Soares_testis_NHT.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of wound healing and disorders of epithelial cell proliferation; particularly chronically open wounds, skin grafting, and cancers of epithelial tissues (e.g. lung and colon cancer). See, e.g., "Wound Healing and Epithelial Cell Proliferation" section, infra. The tissue distribution also indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of cancer and other hyperproliferative disorders (e.g., see "Hyperproliferative Disorders" section, infra).

FEATURES OF PROTEIN ENCODED BY GENE NO: 7

The computer algorithm BLASTX has been used to determine that the translation product of this gene shares sequence homology with, as a non-limiting example, the sequence accessible through the following database accession no. sp|AAF73259|AAF73259 (all information available through the recited accession number is incorporated herein by reference) which is described therein as "Putative seven pass transmembrane protein." Based on the structural similarity these homologous polypeptides are expected to share at least some biological activities. Such activities are known in the art, some of which are described elsewhere herein. Assays for determining such activities are also known in the art, some of which have been described elsewhere herein. Preferred polypeptides of the invention comprise a polypeptide having the amino acid sequence set out in the sequence listing as SEQ ID NO:388.

This gene is expressed in the following tissues/cDNA libraries: Human adult testis, large inserts and to a lesser extent in Soares_testis_NHT; Soares breast 2NbHBst; Soares_placenta_8to9weeks_2NbHP8to9W; Human Adult Testes, Large Inserts, Reexcision; NCI_CGAP_Brn25; NCI_CGAP_Kid3; Soares_NFL_T_GBC_S1; Soares placenta Nb2HP; Soares_NhHMPu_S1; NCI_CGAP_GCB1; Testis 1; NCI_CGAP_Lu19; NCI_CGAP_Co16; NCI_CGAP_Ov23; Hodgkin's Lymphoma I; H. Kidney Cortex, subtracted; Glioblastoma; Human Thymus; Ovarian Tumor 10-3-95; NCI_CGAP_GC4;

Adipocytes; Soares retina N2b4HR; Colon Tumor II; Soares_total_fetus_Nb2HF8_9w; Soares_fetal_liver_spleen_1NFLS_S1; Soares fetal liver spleen 1NFLS; NCI_CGAP_Co21 and NCI_CGAP_Sub5.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of reproductive system disorders; particularly male and female infertility, placental and uterine disorders (e.g. endometriosis), and cancer of reproductive organs (e.g. testicular and ovarian cancer). See "Reproductive System Disorders" section, infra.

FEATURES OF PROTEIN ENCODED BY GENE NO: 8

The computer algorithm BLASTX has been used to determine that the translation product of this gene shares sequence homology with, as a non-limiting example, the sequence accessible through the following database accession no. sp|Q92508|Q92508 (all information available through the recited accession number is incorporated herein by reference) which is described therein as "MYELOBLAST KIAA0233". Based on the structural similarity these homologous polypeptides are expected to share at least some biological activities. Such activities are known in the art, some of which are described elsewhere herein. Assays for determining such activities are also known in the art, some of which have been described elsewhere herein. Preferred polypeptides of the invention comprise a polypeptide having the amino acid sequence set out in the sequence listing as SEQ ID NO:389 .

This gene is expressed in the following tissues/cDNA libraries: Human Pancreas Tumor, Reexcision; Human Amygdala; Soares infant brain 1NIB.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of endocrine system disorders; particularly diabetes and endocrine organ cancers (e.g. pancreatic cancer). See "Endocrine Disorders" section, infra. The tissue distribution also indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of neurological disorders; particularly brain cancer and neurodegenerative

disorders (such as Alzheimer's, Parkinson's and Huntington's Disease). See "Neural Activity and Neurological Diseases" section, infra.

FEATURES OF PROTEIN ENCODED BY GENE NO: 9

The computer algorithm BLASTX has been used to determine that the translation product of this gene shares sequence homology with, as a non-limiting example, the sequence accessible through the following database accession no. sp|Q9ULK5|Q9ULK5 (all information available through the recited accession number is incorporated herein by reference). Based on the structural similarity these homologous polypeptides are expected to share at least some biological activities. Such activities are known in the art, some of which are described elsewhere herein. Assays for determining such activities are also known in the art, some of which have been described elsewhere herein. Preferred polypeptides of the invention comprise a polypeptide having the amino acid sequence set out in the sequence listing as SEQ ID NO:390.

This gene is expressed in the following tissues/cDNA libraries: Human Osteoclastoma Stromal Cells - unamplified and to a lesser extent in NCI_CGAP_Lu24; NCI_CGAP_Gas4; NCI_CGAP_Co3; Human Endometrial Tumor; Activated T-cell(12h)/Thiouridine-re-excision; Soares fetal liver spleen 1NFLS; NCI_CGAP_Kid12; Jurkat T-Cell, S phase; NCI_CGAP_Ut1; NCI_CGAP_Pr28; Human Pancreas Tumor; Human Thymus; NCI_CGAP_Kid11; Human Testes Tumor; NCI_CGAP_GC6; Human Fetal Heart; CD34 positive cells (Cord Blood); Human 8 Week Whole Embryo; Nine Week Old Early Stage Human; Soares_fetal_liver_spleen_1NFLS_S1; Soares_NFL_T_GBC_S1; Soares_testis_NHT and NCI_CGAP_Co19.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of hematopoietic disorders; particularly anemias, clotting disorders/abnormalities (e.g. hemophilia, myocardial infarction, stroke), and leukemia. See "Blood Related Disorders" section, infra. The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the

diagnosis, prevention, and/or treatment of immune system disorders; particularly immune cell proliferative disorders (e.g. leukemia), autoimmune disorders, and immunodeficiencies (including immunodeficiencies caused by genetic factors, microbial pathogens (e.g. HIV), chemotherapy, and radiation). See "Immune Activity" section, infra.

FEATURES OF PROTEIN ENCODED BY GENE NO: 10

This gene is expressed in the following tissues/cDNA libraries: Soares infant brain 1NIB and to a lesser extent in Soares fetal liver spleen 1NFLS; Soares_testis_NHT; Soares_NhHMPu_S1; Early Stage Human Brain; Human Endometrial Tumor; Soares_fetal_lung_NbHL19W; NCI_CGAP_Kid11; Colon Carcinoma; Soares adult brain N2b5HB55Y; H. Frontal cortex,epileptic,re-excision; Soares_pregnant_uterus_NbHPU; Soares_fetal_heart_NbHH19W; NCI_CGAP_GC6; NCI_CGAP_Brn25; Human Amygdala; Human 8 Week Whole Embryo; Pancreas Islet Cell Tumor; Soares_senescent_fibroblasts_NbHSF; Soares_multiple_sclerosis_2NbHMSP; normalized infant brain cDNA; WI 38 cells; Human Manic Depression Tissue; Ovary, Normal: (9805C040R); NCI_CGAP_Pan1; CHME Cell Line,untreated; NCI_CGAP_GC4; Stratagene lung (#937210); NCI_CGAP_Kid5; Colon Tumor II; Soares_total_fetus_Nb2HF8_9w; Soares placenta Nb2HP; NCI_CGAP_Sub3; Human Fetal Brain, normalized A5002F; Human Fetal Brain, normalized C500H; Stratagene corneal stroma (#937222); NCI_CGAP_Lu19; Ovarian Tumor I, OV5232; Human 8 Week Whole Embryo, subtracted; NCI_CGAP_Ov32; NCI_CGAP_GC2; Human Fetal Brain; Jia bone marrow stroma; NCI_CGAP_Br1.1; H. Whole Brain #2, re-excision; Human endometrial stromal cells-treated with estradiol; NCI_CGAP_Co9; Human normal ovary(#9610G215); Glioblastoma; NCI_CGAP_Co14; Human Infant Brain; Stratagene muscle 937209; NCI_CGAP_Pr22; Human T-cell lymphoma,re-excision; Ovary, Cancer: (15799A1F) Poorly differentiated carcinoma; Stratagene pancreas (#937208); NCI_CGAP_Pr28; NCI_CGAP_Gas4; Human Hypothalmus,Schizophrenia; Stratagene endothelial cell 937223; Human Hippocampus; Soares_NSF_F8_9W_OT_PA_P_S1; Human Rhabdomyosarcoma; NCI_CGAP_CLL1; Human Testes Tumor, re-excision; Human Placenta (re-

excision); Human adult testis, large inserts; Human endometrial stromal cells-treated with progesterone; NCI_CGAP_Co8; Human Pancreas Tumor, Reexcision; Bone marrow; T-Cell PHA 16 hrs; Soares retina N2b4HR; NCI_CGAP_Brn23; Human Adult Heart,re-excision; Human fetal heart, Lambda ZAP Express; T-Cell PHA 24 hrs; Neutrophils IL-1 and LPS induced; Human Bone Marrow, treated; Soares melanocyte 2NbHM; Nine Week Old Early Stage Human; T cell helper II; Human Cerebellum; Soares_fetal_liver_spleen_1NFLS_S1; NCI_CGAP_GU1; NCI_CGAP_Co19 and NCI_CGAP_Sub6.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of neurological disorders; particularly brain cancer and neurodegenerative disorders (such as Alzheimer's, Parkinson's and Huntington's Disease). See "Neural Activity and Neurological Diseases" section, infra. The tissue distribution also indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of cancer and other hyperproliferative disorders (e.g., see "Hyperproliferative Disorders" section, infra).

FEATURES OF PROTEIN ENCODED BY GENE NO: 12

This gene is expressed in Human Thymus Stromal Cells.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of immune system disorders; particularly immune cell proliferative disorders (e.g. leukemia), autoimmune disorders, and immunodeficiencies (including immunodeficiencies caused by genetic factors, microbial pathogens (e.g. HIV), chemotherapy, and radiation). See "Immune Activity" section, infra.

FEATURES OF PROTEIN ENCODED BY GENE NO: 13

The computer algorithm BLASTX has been used to determine that the translation product of this gene shares sequence homology with, as a non-limiting

example, the sequence accessible through the following database accession no. sp|BAA91131|BAA91131 (all information available through the recited accession number is incorporated herein by reference). Based on the structural similarity these homologous polypeptides are expected to share at least some biological activities. Such activities are known in the art, some of which are described elsewhere herein. Assays for determining such activities are also known in the art, some of which have been described elsewhere herein. Preferred polypeptides of the invention comprise a polypeptide having the amino acid sequence set out in the sequence listing as SEQ ID NO: 392, SEQ ID NO: 393, SEQ ID NO: 394, SEQ ID NO: 395, and SEQ ID NO: 395.

This gene is expressed in the following tissues/cDNA libraries: Resting T-Cell Library,II; Human Activated T-Cells, re-excision; Activated T-cell(12h)/Thiouridine-re-excision; NCI_CGAP_Sub3.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of immune system disorders; particularly immune cell proliferative disorders (e.g. leukemia), autoimmune disorders, and immunodeficiencies (including immunodeficiencies caused by genetic factors, microbial pathogens (e.g. HIV), chemotherapy, and radiation). See "Immune Activity" section, infra.

FEATURES OF PROTEIN ENCODED BY GENE NO: 14

The computer algorithm BLASTX has been used to determine that the translation product of this gene shares sequence homology with, as a non-limiting example, the sequence accessible through the following Genbank protein database accession no. pir|S41408|S41408 (all information available through the recited accession number is incorporated herein by reference) which is described therein as "lysosomal acid lipase (EC 3.1.1.-) / sterol esterase (EC 3.1.1.13) precursor - human. Based on the structural similarity these homologous polypeptides are expected to share at least some biological activities. Such activities are known in the art, some of which are described elsewhere herein. Assays for determining such activities are also

known in the art, some of which have been described elsewhere herein. Preferred polypeptides of the invention comprise a polypeptide having the amino acid sequence set out in the sequence listing as SEQ ID NO: 397 and/or SEQ ID NO: 398 . The protein encoded by this clone is ~40% identical to lipase (NP_000226.1) and similarly identical to gastic lipase (NP_004181.1).

This gene is expressed in Healing groin wound - zero hr post-incision (control).

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of wound healing and disorders of epithelial cell proliferation; particularly chronically open wounds, skin grafting, and cancers of epithelial tissues (e.g. lung and colon cancer). See "Wound Healing and Epithelial Cell Proliferation" section, infra. The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of diseases of lipid metabolism, cholesterol storage disease, Wolman disease, atherosclerosis, and/or coronary artery disease.

The protein encoded by this clone is ~40% identical to lipase A, the lysosomal acid lipase (also known as cholesteyrl ester hydrolase). This enzyme functions in the lysosome to catalyze the hydrolysis of cholesteryl esters and triglycerides. Mutations in LIPA can result in Wolman disease and cholesteryl ester storage disease. Human lysosomal acid lipase (hLAL) is essential for the hydrolysis of cholesteryl esters and triglycerides in the lysosome. Defective hLAL activity leads to two autosomal recessive traits, Wolman disease (WD) or cholesteryl ester storage disease (CESD). Phenotypically, WD has accumulation of both triglycerides and cholesteryl esters, while CESD has mainly elevated cholesteryl esters.

FEATURES OF PROTEIN ENCODED BY GENE NO: 15

The computer algorithm BLASTX has been used to determine that the translation product of this gene shares sequence homology with, as a non-limiting example, the sequence accessible through the following database accession no. sp|BAB01630|BAB01630 (all information available through the recited accession

number is incorporated herein by reference) which is described therein as "Unnamed protein product." Based on the structural similarity these homologous polypeptides are expected to share at least some biological activities. Such activities are known in the art, some of which are described elsewhere herein. Assays for determining such activities are also known in the art, some of which have been described elsewhere herein. Preferred polypeptides of the invention comprise a polypeptide having the amino acid sequence set out in the sequence listing as SEQ ID NO: 399 and/or SEQ ID NO: 400.

This gene is expressed in Dendritic Cells From CD34 Cells.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of immune system disorders; particularly immune cell proliferative disorders (e.g. leukemia), autoimmune disorders, and immunodeficiencies (including immunodeficiencies caused by genetic factors, microbial pathogens (e.g. HIV), chemotherapy, and radiation). See "Immune Activity" section, infra.

FEATURES OF PROTEIN ENCODED BY GENE NO: 16

This gene is expressed in the following tissues/cDNA libraries: NCI_CGAP_Pr28 and to a lesser extent in Macrophage-oxLDL; Epithelial-TNFa and INF induced; Stratagene colon (#937204); Human Neutrophil, Activated; Human Adult Pulmonary,re-excision; Human Testes; Soares_testis_NHT; Primary Dendritic Cells, lib 1; Macrophage-oxLDL, re-excision; Prostate Adenocarcinoma; NCI_CGAP_Co16; Human Pancreatic Carcinoma; Breast, Cancer: (4004943 A5); Human Neutrophil; NCI_CGAP_Ew1; NCI_CGAP_Pr22; Stratagene fetal retina 937202; NCI_CGAP_Br2; NCI_CGAP_CLL1; Human adult testis, large inserts; Fetal Liver, subtraction II; Rectum tumour; Human Adult Testes, Large Inserts, Reexcision; Rejected Kidney, lib 4; Human blood platelets; CD34 depleted Buffy Coat (Cord Blood), re-excision; NCI_CGAP_Kid5; Monocyte activated; Human Bone Marrow, treated; Soares ovary tumor NbHOT; Dendritic cells, pooled; neutrophils control; Keratinocyte; Colon Tumor II and NCI_CGAP_Sub2.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of immune system disorders; particularly immune cell proliferative disorders (e.g. leukemia), autoimmune disorders, and immunodeficiencies (including immunodeficiencies caused by genetic factors, microbial pathogens (e.g. HIV), chemotherapy, and radiation). See "Immune Activity" section, infra. The tissue distribution also indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of cancer and other hyperproliferative disorders (e.g., see "Hyperproliferative Disorders" section, infra).

FEATURES OF PROTEIN ENCODED BY GENE NO: 17

This gene is expressed in Human Stomach, re-excision.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of gastrointestinal system disorders; particularly inflammatory diseases (e.g. gastroenteritis and stomach ulcers) and gastrointestinal cancers (e.g. stomach and colon cancer. See "Gastrointestinal Disorders" section, infra.

FEATURES OF PROTEIN ENCODED BY GENE NO: 18

The computer algorithm BLASTX has been used to determine that the translation product of this gene shares sequence homology with, as a non-limiting example, the sequence accessible through the following database accession no. pir|A26829|ISBOSS (all information available through the recited accession number is incorporated herein by reference) which is described therein as "protein disulfide-isomerase (EC 5.3.4.1) precursor - bovine". Based on the structural similarity these homologous polypeptides are expected to share at least some biological activities. Such activities are known in the art, some of which are described elsewhere herein. Assays for determining such activities are also known in the art, some of which have been described elsewhere herein. Preferred polypeptides of the invention comprise a

polypeptide having the amino acid sequence set out in the sequence listing as SEQ ID NO: 401.

This gene is expressed in the following tissues/cDNA libraries: Pancreas Tumor PCA4 Tu and to a lesser extent in Ovary, Cancer: (4004562 B6) Papillary Serous Cystic Neoplasm, Low Malignant Pot; Pancreas normal PCA4 No; Soares fetal liver spleen 1NFLS; NCI_CGAP_Ut4; NCI_CGAP_Kid11; Soares_parathyroid_tumor_NbHPA; NCI_CGAP_GCB1; H. Kidney Medulla, subtracted; HPAS (human pancreas, subtracted); NCI_CGAP_Ov23; NCI_CGAP_Thy1; Ovarian Cancer; Breast, Cancer: (4004943 A5); NCI_CGAP_Ut1; Human Pancreas Tumor; NCI_CGAP_CLL1; Palate normal; Human Pancreas Tumor, Reexcision; Soares_fetal_lung_NbHL19W; Soares_fetal_liver_spleen_1NFLS_S1 and Soares_NhHMPu_S1.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of endocrine system disorders; particularly diabetes and endocrine organ cancers (e.g. pancreatic cancer). See, e.g., "Endocrine Disorders" section, infra. The tissue distribution also indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of cancer and other hyperproliferative disorders (e.g., see "Hyperproliferative Disorders" section, infra).

FEATURES OF PROTEIN ENCODED BY GENE NO: 19

The computer algorithm BLASTX has been used to determine that the translation product of this gene shares sequence homology with, as a non-limiting example, the sequence accessible through the following Genbank database accession no. pir|T42691|T42691 (all information available through the recited accession number is incorporated herein by reference) which is described therein as "hypothetical protein DKFZp434D2328.1 - human (fragment)". Based on the structural similarity these homologous polypeptides are expected to share at least some biological activities. Such activities are known in the art, some of which are described elsewhere herein. Assays for determining such activities are also known in

the art, some of which have been described elsewhere herein. Preferred polypeptides of the invention comprise a polypeptide having the amino acid sequence set out in the sequence listing as SEQ ID NO: 402 and/or SEQ ID NO: 403.

This gene is expressed in CHME Cell Line, treated 5 hrs.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include but are not limited to: Alzheimer's disease. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the nervous system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., neuronal, cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The elevated level of expression in microglial cells indicates that the protein product of this clone would be useful for the detection/treatment of neurodegenerative disease states and behavioral disorders such as Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder and panic disorder.

FEATURES OF PROTEIN ENCODED BY GENE NO: 20

This sequence matches UniGene cluster Hs.127376, which maps to chromosome 13.

This gene is expressed in the following tissues/cDNA libraries: Human Rhabdomyosarcoma; normalized infant brain cDNA; Soares_testis_NHT and to a lesser extent in Soares placenta Nb2HP; NCI_CGAP_Kid11; Soares melanocyte 2NbHM; Soares_NFL_T_GBC_S1; NCI_CGAP_GCB1; Normal Human Trabecular Bone Cells; NCI_CGAP_Br2; Hepatocellular Tumor, re-excision; Palate carcinoma;

Soares_NhHMPu_S1; Soares infant brain 1NIB; Larynx carcinoma IV; Stomach Tumour; Thymus; NCI_CGAP_Co16; NCI_CGAP_Kid8; Activated T-cells; NCI_CGAP_Ut4; B Cell lymphoma; wilm's tumor; HEL cell line; NCI_CGAP_Ut2; Human Adult Small Intestine; NCI_CGAP_Ut1; NCI_CGAP_Pr22; Epithelial-TNFa and INF induced; Rejected Kidney, lib 4; Ovary, Cancer (9809C332): Poorly differentiated adenocarcinoma; Normal colon; NCI_CGAP_GC6; Pancreas Islet Cell Tumor; NCI_CGAP_Kid3; Soares_multiple_sclerosis_2NbHMSP; Dendritic cells, pooled; Colon Tumor II; Soares_pregnant_uterus_NbHPU and NCI_CGAP_Sub4.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of neurological disorders; particularly brain cancer and neurodegenerative disorders (such as Alzheimer's, Parkinson's and Huntington's Disease). See "Neural Activity and Neurological Diseases" section, infra. The tissue distribution also indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of cancer and other hyperproliferative disorders (e.g., see "Hyperproliferative Disorders" section, infra).

FEATURES OF PROTEIN ENCODED BY GENE NO: 21

This gene is expressed in the following tissues/cDNA libraries: Pancreas Islet Cell Tumor; Soares_parathyroid_tumor_NbHPA and to a lesser extent in NCI_CGAP_Brn52; NCI_CGAP_Ut3; Human Soleus; Stratagene muscle 937209; Palate normal; Human Adult Heart,re-excision; NTERA2 teratocarcinoma cell line+retinoic acid (14 days) and Soares_NhHMPu_S1.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of endocrine system disorders; particularly diabetes and endocrine organ cancers (e.g. pancreatic cancer). See "Endocrine Disorders" section, infra. The tissue distribution also indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or

treatment of cancer and other hyperproliferative disorders (e.g., see "Hyperproliferative Disorders" section, infra).

FEATURES OF PROTEIN ENCODED BY GENE NO: 22

The computer algorithm BLASTX has been used to determine that the translation product of this gene shares sequence homology with, as a non-limiting example, the sequence accessible through the following database accession no. sp|BAA95033|BAA95033 (all information available through the recited accession number is incorporated herein by reference) which is described therein as "Brain cDNA, clone MNCb-3816, similar to AF171875 g1-related zinc finger protein (Mus musculus)." Based on the structural similarity these homologous polypeptides are expected to share at least some biological activities. Such activities are known in the art, some of which are described elsewhere herein. Assays for determining such activities are also known in the art, some of which have been described elsewhere herein. Preferred polypeptides of the invention comprise a polypeptide having the amino acid sequence set out in the sequence listing as SEQ ID NO:404.

This gene is expressed in the following tissues/cDNA libraries: NCI_CGAP_Co11; Soares placenta Nb2HP and to a lesser extent in Human fetal brain (TFujiwara); Hepatocellular Tumor; NCI_CGAP_Co14; Clontech human aorta polyA+ mRNA (#6572); Stratagene liver (#937224); NCI_CGAP_Pan1; NCI_CGAP_Kid11; Colon Normal II; Soares fetal liver spleen 1NFLS; Human adult small intestine,re-excision; Hepatocellular Tumor,re-excision; Human Colon Cancer,re-excision; Human Stomach,re-excision; Human Osteoclastoma, re-excision; Morton Fetal Cochlea; Stratagene pancreas (#937208); Liver, Hepatoma; Liver Tumour Met 5 Tu; Hepatocellular Tumor, re-excision; Human Placenta (re-excision); Human Liver, normal; 12 Week Old Early Stage Human; Colon Tumor; Rectum tumour; Stomach Normal; Human Pancreas Tumor, Reexcision; Human Endometrial Tumor and NCI_CGAP_GU1.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of cancer and other

hyperproliferative disorders (e.g., see "Hyperproliferative Disorders" section, infra). The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of neurological disorders; particularly brain cancer and neurodegenerative disorders (such as Alzheimer's, Parkinson's and Huntington's Disease). See "Neural Activity and Neurological Diseases" section, infra. Furthermore, the tissue distribution indicates polynucleotides and polypeptides corresponding to this gene would be useful for the diagnosis, prevention, and or treatment of liver disorders and cancers. For example, the protein can be used for the detection, treatment, and/or prevention of Wilson's disease, cirrhosis, fibrosis, bilirubin metabolism, hepatomegaly, cholestasis, liver cancer (for example, hepatoblastoma), jaundice, hepatitis (acuta and chronic) and liver metabolic diseases and conditions attributable to the differentiation of hepatocyte progenitor cells.

FEATURES OF PROTEIN ENCODED BY GENE NO: 23

This gene is expressed in Colon Normal.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of gastrointestinal system disorders; particularly inflammatory diseases (e.g. gastroenteritis and stomach ulcers) and gastrointestinal cancers (e.g. stomach and colon cancer. See "Gastrointestinal Disorders" section, infra.

FEATURES OF PROTEIN ENCODED BY GENE NO: 24

This gene is expressed most predominantly in fetal heart. It is also expressed in hemangiopericytoma, a neoplasm derived from pericytes, the cells normally arranged along capillaries and venuels. Other tissues expressing this cDNA include: NCI_CGAP_Pr28;NCI_CGAP_Brn35;NCI_CGAP_Ov23;Frontal lobe,dementia;re-excision;CD34 positive cells (cord blood),re-ex;NCI_CGAP_Ut2; Adipose tissue (diabetic type II)#41689;NCI_CGAP_Pr1;NCI_CGAP_Ut1;Healing groin wound - zero hr post-incision (control);Human Fetal Dura Mater;Human T-Cell Lymphoma;Palate carcinoma;NCI_CGAP_GC4;Rejected Kidney, lib

4;NCI_CGAP_GC6;Human Fetal Lung III;T-Cell PHA 16 hrs;Soares_placenta_8to9weeks_2NbHP8to9W;Colon Normal;NCI_CGAP_Lu5;Soares_fetal_lung_NbHL19W;Soares_total_fetus_Nb2HF8_9w;Soares_pregnant_uterus_NbHPU;Soares_NhHMPu_S1;NCI_CGAP_GCB1;NCI_CGAP_GU1;NCI_CGAP_Brn53.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of cancer and other proliferative disorders as well as type II diabetes. Accordingly, polynucleotides and/or polypeptides of the invention and/or antagonists thereof (especially neutralizing or antagonistic antibodies) may be used to treat, prevent, and/or ameliorate type II diabetes. Additionally, in other embodiments, the polynucleotides and/or polypeptides corresponding to this gene and/or antagonists thereof (especially neutralizing or antagonistic antibodies) may be used to treat, prevent, or ameliorate conditions associated with type II diabetes mellitus, including, but not limited to, seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, kidney disease (e.g., renal failure, nephropathy other diseases and disorders as described in the "Renal Disorders" section below), endocrine disorders (as described in the "Endocrine Disorders" section below), obesity, nerve damage, neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, infections (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture. In another embodiment, the polynucleotides and/or polypeptides of the invention and/or antagonists thereof (especially neutralizing or antagonistic antibodies) may be used to treat, prevent, and/or ameliorate diabetes and/or complication associated with diabetes. Complications associated with diabetes include: blindness (e.g., due to diabetic retinopathy), kidney disease (e.g., due to diabetic nephropathy), nerve disease (e.g., due to diabetic neuropathy) and amputations, heart disease and stroke, and impotence (e.g., due to diabetic neuropathy or blood vessel blockage. In additional preferred embodiments,

polypeptides, polynucleotides, antibodies, agonists, or antagonists corresponding to that polypeptide, may be used to regulate weight gain, weight loss, and/or obesity. In other embodiments, the polynucleotides and/or polypeptides of the invention and/or antagonists thereof (especially neutralizing or antagonistic antibodies) may be used to treat, prevent, and/or ameliorate other diseases or disorders described herein (See, e.g.,. "Biological Activities" section and the sections cross-referenced therein).

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of wound healing and disorders of epithelial cell proliferation; particularly chronically open wounds, skin grafting, and cancers of epithelial tissues (e.g. lung and colon cancer). See "Wound Healing and Epithelial Cell Proliferation" section, infra.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of heart disease as well as other diseases of the vasculature. This factor (or antibodies raised against it) may be useful as a anti- or pro-angiogenic therapeutics for such diseases as cancer, ischemia, stroke, and cardiovascular disease.

This cDNA is expressed in highly vascularized tissues (fetal heart, hemangiopericytoma, brain, healing wound, and numerous tumor types). This tissue distribution is suggestive of a factor involved in angiogenesis.

FEATURES OF PROTEIN ENCODED BY GENE NO: 25

This gene is expressed in the following tissues/cDNA libraries: Human Testes Tumor and to a lesser extent in Human Whole Brain #2 - Oligo dT > 1.5Kb; HEL cell line; Stratagene NT2 neuronal precursor 937230; Human Adrenal Gland Tumor; Human Testes Tumor, re-excision; Myoloid Progenitor Cell Line; Human Bone Marrow, treated; NTERA2 teratocarcinoma cell line+retinoic acid (14 days); Human 8 Week Whole Embryo; Activated T-cell(12h)/Thiouridine-re-excision; NCI_CGAP_GCB1 and Primary Dendritic Cells, lib 1.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of reproductive system disorders; particularly male and female infertility, placental and uterine disorders (e.g. endometriosis), and cancer of reproductive organs (e.g. testicular and ovarian cancer). See "Reproductive System Disorders" section, infra. The tissue distribution also indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of neurological disorders; particularly brain cancer and neurodegenerative disorders (such as Alzheimer's, Parkinson's and Huntington's Disease). See "Neural Activity and Neurological Diseases" section, infra. Moreover, the tissue distribution also indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of cancer and other hyperproliferative disorders (e.g., see "Hyperproliferative Disorders" section, infra).

FEATURES OF PROTEIN ENCODED BY GENE NO: 26

This gene is expressed in Human T-cell lymphoma,re-excision.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of immune system disorders; particularly immune cell proliferative disorders (e.g. leukemia), autoimmune disorders, and immunodeficiencies (including immunodeficiencies caused by genetic factors, microbial pathogens (e.g. HIV), chemotherapy, and radiation). See "Immune Activity" section, infra.

FEATURES OF PROTEIN ENCODED BY GENE NO: 27

The computer algorithm BLASTX has been used to determine that the translation product of this gene shares sequence homology with, as a non-limiting example, the sequence accessible through the following database accession no. sp|BAA95074|BAA95074 (all information available through the recited accession number is incorporated herein by reference) which is described therein as "Brain

cDNA, clone MNCb-2717." Based on the structural similarity these homologous polypeptides are expected to share at least some biological activities. Such activities are known in the art, some of which are described elsewhere herein. Assays for determining such activities are also known in the art, some of which have been described elsewhere herein. Preferred polypeptides of the invention comprise a polypeptide having the amino acid sequence set out in the sequence listing as SEQ ID NO: 407 .

This gene is expressed in the following tissues/cDNA libraries: CHME Cell Line,treated 5 hrs; NTERA2 teratocarcinoma cell line+retinoic acid (14 days).

The protein homology indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of neurological disorders; particularly brain cancer and neurodegenerative disorders (such as Alzheimer's, Parkinson's and Huntington's Disease). See "Neural Activity and Neurological Diseases" section, infra. The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of cancer and other hyperproliferative disorders (e.g., see "Hyperproliferative Disorders" section, infra).

FEATURES OF PROTEIN ENCODED BY GENE NO: 28

The computer algorithm BLASTX has been used to determine that the translation product of this gene shares sequence homology with, as a non-limiting example, the sequence accessible through the following database accession no. sp|BAA91877|BAA91877 (all information available through the recited accession number is incorporated herein by reference). Based on the structural similarity these homologous polypeptides are expected to share at least some biological activities. Such activities are known in the art, some of which are described elsewhere herein. Assays for determining such activities are also known in the art, some of which have been described elsewhere herein. Preferred polypeptides of the invention comprise a polypeptide having the amino acid sequence set out in the sequence listing as SEQ ID NO: 408 .

This gene is expressed in the following tissues/cDNA libraries: Soares infant brain 1NIB and to a lesser extent in Soares_NhHMPu_S1; Soares_total_fetus_Nb2HF8_9w; Soares_fetal_liver_spleen_1NFLS_S1; Ovary, Cancer(4004650 A3): Well-Differentiated Micropapillary Serous Carcinoma; NCI_CGAP_Lu5; normalized infant brain cDNA; Colon Tumor II; NCI_CGAP_Pr28; NCI_CGAP_Gas4; NCI_CGAP_Kid11; Pancreas normal PCA4 No; 12 Week Early Stage Human II, Reexcision; Soares_testis_NHT; Synovial IL-1/TNF stimulated; Synovial hypoxia; NCI_CGAP_Ut1; Human Placenta (re-excision); Human Ovary; Palate carcinoma; Stomach Normal; Stratagene lung (#937210); Prostate Adenocarcinoma; Soares ovary tumor NbHOT; NCI_CGAP_GCB1; Human adult lung 3' directed MboI cDNA; NK Cells (NKYao20 Control); Pharynx carcinoma; human colon cancer; Smooth muscle, control, re-excision; STRATAGENE Human skeletal muscle cDNA library, cat. #936215.; NCI_CGAP_Ut3; NCI_CGAP_AA1; Ovarian cancer, Serous Papillary Adenocarcinoma; Human Ovarian Cancer(#9807G017); Hepatocellular Tumor; Ku 812F Basophils Line; Ovarian cancer, Serous Papillary Adenocarcinoma; Salivary Gland, Lib 2; Ovarian Cancer, # 9702G001; Synovial Fibroblasts (Il1/TNF), subt; H. Meningima, M1; Breast, Cancer: (4004943 A5); Stratagene lung carcinoma 937218; Spinal Cord, re-excision; Monocyte activated, re-excision; Human Umbilical Vein Endothelial Cells, uninduced; Human Fetal Dura Mater; Ovary, Normal: (9805C040R); Ovary, Cancer (15395A1F): Grade II Papillary Carcinoma; Soares breast 2NbHBst; Human Adipose; NCI_CGAP_Pan1; Liver Normal Met5No; Ovary, Cancer: (4004576 A8); Colon, normal; Rectum tumour; Human Testes Tumor; Normal colon; NCI_CGAP_GC6; Human Ovarian Cancer Reexcision; Human Osteoclastoma; NCI_CGAP_Kid3; Monocyte activated; HUMAN B CELL LYMPHOMA; Spleen, Chronic lymphocytic leukemia; Bone Marrow Cell Line (RS4,11); Human Testes; Dendritic cells, pooled; NTERA2 teratocarcinoma cell line+retinoic acid (14 days); Soares_parathyroid_tumor_NbHPA; Soares melanocyte 2NbHM; Nine Week Old Early Stage Human; Soares_fetal_lung_NbHL19W; T cell helper II; Soares_NFL_T_GBC_S1; Soares placenta Nb2HP; Primary Dendritic Cells, lib 1; NCI_CGAP_Sub6; NCI_CGAP_Brn53 and NCI_CGAP_Kid13.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of neurological disorders; particularly brain cancer and neurodegenerative disorders (such as Alzheimer's, Parkinson's and Huntington's Disease). See "Neural Activity and Neurological Diseases" section, infra. The tissue distribution also indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of cancer and other hyperproliferative disorders (e.g., see "Hyperproliferative Disorders" section, infra).

FEATURES OF PROTEIN ENCODED BY GENE NO: 29

This gene is expressed in Human Ovarian Cancer Reexcision.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of reproductive system disorders; particularly male and female infertility, placental and uterine disorders (e.g. endometriosis), and cancer of reproductive organs (e.g. testicular and ovarian cancer). See "Reproductive System Disorders" section, infra. The tissue distribution also indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of cancer and other hyperproliferative disorders (e.g., see "Hyperproliferative Disorders" section, infra).

FEATURES OF PROTEIN ENCODED BY GENE NO: 30

This gene is expressed in PC3 Prostate cell line.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of reproductive system disorders; particularly male and female infertility, placental and uterine disorders (e.g. endometriosis), and cancer of reproductive organs (e.g. testicular and ovarian cancer). See "Reproductive System Disorders" section, infra.

FEATURES OF PROTEIN ENCODED BY GENE NO: 31

This gene is expressed in the following tissues/cDNA libraries: Human Adrenal Gland Tumor; Prostate Adenocarcinoma.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of endocrine system disorders; particularly diabetes and endocrine organ cancers (e.g. pancreatic cancer). See "Endocrine Disorders" section, infra. The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of cancer and other hyperproliferative disorders (e.g., see "Hyperproliferative Disorders" section, infra).

FEATURES OF PROTEIN ENCODED BY GENE NO: 32

The computer algorithm BLASTX has been used to determine that the translation product of this gene shares sequence homology with, as a non-limiting example, the sequence accessible through the following database accession no. sp|Q9VFG7|Q9VFG7 (all information available through the recited accession number is incorporated herein by reference) which is described therein as "CG7530 PROTEIN." Based on the structural similarity these homologous polypeptides are expected to share at least some biological activities. Such activities are known in the art, some of which are described elsewhere herein. Assays for determining such activities are also known in the art, some of which have been described elsewhere herein.

Preferred polypeptides of the invention comprise a polypeptide having the amino acid sequence set out in the sequence listing as SEQ ID NO:409.

This gene is expressed in Human Testes, Reexcision.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of reproductive system disorders; particularly male and female infertility, placental and uterine disorders (e.g.

endometriosis), and cancer of reproductive organs (e.g. testicular and ovarian cancer). See "Reproductive System Disorders" section, infra.

FEATURES OF PROTEIN ENCODED BY GENE NO: 33

This gene is expressed in the following tissues/cDNA libraries: Human Testes Tumor and to a lesser extent in NCI_CGAP_Co14; Activated T-cell(12h)/Thiouridine-re-excision; Soares_testis_NHT; Human adult testis, large inserts; Human Adult Testes, Large Inserts, Reexcision; NCI_CGAP_GC6; Activated T-Cell (12hs)/Thiouridine labelledEco; Human Endometrial Tumor; Soares infant brain 1NIB; Human Chronic Synovitis; NCI_CGAP_Pr28; NCI_CGAP_Co3; Human Pancreas Tumor, Reexcision; Adipocytes; Soares ovary tumor NbHOT; T Cell helper I; NCI_CGAP_Lu5; Keratinocyte; NCI_CGAP_Lu19; Testes; NCI_CGAP_Br3; Whole 6 Week Old Embryo; NCI_CGAP_Eso2; Human Colon, subtraction; Human Fetal Spleen; Human Liver; NCI_CGAP_Ut4; Lung, Cancer (4005313 A3): Invasive Poorly Differentiated Lung Adenocarcinoma;; Human Synovium; Ovarian Cancer, # 9702G001; Human Whole Brain #2 - Oligo dT > 1.5Kb; Stratagene neuroepithelium (#937231); TF-1 Cell Line GM-CSF Treated; Human Fetal Kidney; H. Epididiymus, cauda; Ovary, Cancer: (15799A1F) Poorly differentiated carcinoma; Human Pancreas Tumor; Human Adrenal Gland Tumor; Human Whole Six Week Old Embryo; NCI_CGAP_Pan1; Ovary, Cancer: (4004576 A8); Palate normal; Human T-Cell Lymphoma; Ovarian Tumor 10-3-95; NCI_CGAP_Kid11; Colon Carcinoma; NCI_CGAP_GC4; Ovary, Cancer (9809C332): Poorly differentiated adenocarcinoma; T-Cell PHA 16 hrs; Soares_senescent_fibroblasts_NbHSF; Human Thymus Stromal Cells; Human Bone Marrow, treated; Bone Marrow Cell Line (RS4,11); Soares_parathyroid_tumor_NbHPA; Soares_fetal_lung_NbHL19W; Colon Tumor II; Soares_pregnant_uterus_NbHPU; NCI_CGAP_Br18; NCI_CGAP_CML1 and NCI_CGAP_Sub3.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of reproductive system disorders; particularly male and female infertility, placental and uterine disorders (e.g.

endometriosis), and cancer of reproductive organs (e.g. testicular and ovarian cancer). See "Reproductive System Disorders" section, infra.

FEATURES OF PROTEIN ENCODED BY GENE NO: 34

This gene is expressed in the following tissues/cDNA libraries: Human Adult Testes, Large Inserts, Reexcision; Human adult testis, large inserts.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of reproductive system disorders; particularly male infertility and cancer of reproductive organs (e.g. testicular cancer). See "Reproductive System Disorders" section, infra.

FEATURES OF PROTEIN ENCODED BY GENE NO: 35

This gene is expressed in human tonsils.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of immune system disorders; particularly immune cell proliferative disorders (e.g. leukemia), autoimmune disorders, and immunodeficiencies (including immunodeficiencies caused by genetic factors, microbial pathogens (e.g. HIV), chemotherapy, and radiation). See "Immune Activity" section, infra.

FEATURES OF PROTEIN ENCODED BY GENE NO: 36

This gene is expressed in the following tissues/cDNA libraries: Human Activated T-Cells, re-excision; Human Pancreas Tumor, Reexcision.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of immune system disorders; particularly immune cell proliferative disorders (e.g. leukemia), autoimmune disorders, and immunodeficiencies (including immunodeficiencies caused by genetic factors, microbial pathogens (e.g. HIV), chemotherapy, and radiation). See "Immune Activity" section, infra. The tissue distribution also indicates polynucleotides and

polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of endocrine system disorders; particularly diabetes and endocrine organ cancers (e.g. pancreatic cancer). See "Endocrine Disorders" section, infra.

FEATURES OF PROTEIN ENCODED BY GENE NO: 37

The computer algorithm BLASTX has been used to determine that the translation product of this gene shares sequence homology with, as a non-limiting example, the sequence accessible through the following Genbank database accession no. sp|Q9Z0T1|Q9Z0T1 (all information available through the recited accession number is incorporated herein by reference) which is described therein as "HYPOTHETICAL 18.9 KDA PROTEIN (FRAGMENT)." Based on the structural similarity these homologous polypeptides are expected to share at least some biological activities. Such activities are known in the art, some of which are described elsewhere herein. Assays for determining such activities are also known in the art, some of which have been described elsewhere herein. Preferred polypeptides of the invention comprise a polypeptide having the amino acid sequence set out in the sequence listing as SEQ ID NO:410 .

This gene is expressed in the following tissues/cDNA libraries: NCI_CGAP_Gas4 and to a lesser extent in Smooth muscle, serum treated; Soares_pregnant_uterus_NbHPU; Soares placenta Nb2HP; NCI_CGAP_Pan1; Primary Dendritic Cells, lib 1; Smooth muscle, serum induced,re-exc; Soares_placenta_8to9weeks_2NbHP8to9W; Hodgkin's Lymphoma II; Soares fetal liver spleen 1NFLS; Human Adipose Tissue, re-excision; NCI_CGAP_Kid3; Smooth muscle,control; Soares_NFL_T_GBC_S1; Human Pituitary, subtracted; H. Kidney Cortex, subtracted; H. Epididiymus, cauda; Soares breast 2NbHBst; Human Whole Six Week Old Embryo; NCI_CGAP_Kid5; Colon Tumor II; NCI_CGAP_Lu28; Human osteoarthritic,fraction II; Liver HepG2 cell line.; Lung, Normal: (4005313 B1); NCI_CGAP_Kid8; Hepatocellular Tumor; Synovial hypoxia-RSF subtracted; Human Chronic Synovitis; NCI_CGAP_Ut1; LPS activated derived dendritic cells; Ovary, Normal: (9805C040R); Stratagene endothelial cell 937223; L428; Human Ovary; Human Gall Bladder; Soares breast 3NbHBst; NCI_CGAP_GC4; Human

Pancreas Tumor, Reexcision; Human Synovial Sarcoma; Human Placenta; Pancreas normal PCA4 No; NCI_CGAP_Brn23; Human Placenta; HUMAN B CELL LYMPHOMA; NCI_CGAP_Lu5; H. Frontal cortex,epileptic,re-excision; Soares melanocyte 2NbHM; Soares_testis_NHT; Human Pituitary, subtracted V; NCI_CGAP_Mel3; Human Pituitary; Bone marrow stroma,treated; NCI_CGAP_Lu19; Human fetal lung; NCI_CGAP_Eso2; Human White Adipose; Hep G2 Cells, PCR library; Pancreatic Islet; Human Pancreatic Carcinoma; HUMAN STOMACH; Frontal lobe,dementia,re-excision; Human Fetal Bone; Amniotic Cells - TNF induced; Early Stage Human Lung, subtracted; Human Lung; Lung, Cancer (4005163 B7): Invasive, Poorly Diff. Adenocarcinoma, Metastatic; Smooth Muscle-HASTE normalized; Human Normal Breast; NCI_CGAP_AA1; Human Synovium; Human Umbilical Vein, Endo. remake; Ovarian cancer, Serous Papillary Adenocarcinoma; Synovial Fibroblasts (Il1/TNF), subt; Synovial hypoxia; Human Pituitary, subt IX; NCI_CGAP_Ut2; HM1; Human Pancreas Tumor; Human Dermal Endothelial Cells,untreated; CD40 activated monocyte dendridic cells; Human Adipose; Stratagene liver (#937224); NCI_CGAP_Co3; Human Placenta (re-excision); 12 Week Old Early Stage Human; NCI_CGAP_Kid11; Adipocytes; Human Fetal Lung III; Endothelial-induced; Primary Dendritic cells,frac 2; NCI_CGAP_Brn25; Osteoblasts; Soares_parathyroid_tumor_NbHPA; Soares_total_fetus_Nb2HF8_9w; Soares_fetal_liver_spleen_1NFLS_S1 and NCI_CGAP_Sub3.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of cancer and other hyperproliferative disorders (e.g., see "Hyperproliferative Disorders" section, infra).

FEATURES OF PROTEIN ENCODED BY GENE NO: 38

This gene is expressed in T cell helper II.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of immune system disorders;

particularly immune cell proliferative disorders (e.g. leukemia), autoimmune disorders, and immunodeficiencies (including immunodeficiencies caused by genetic factors, microbial pathogens (e.g. HIV), chemotherapy, and radiation). See "Immune Activity" section, infra.

FEATURES OF PROTEIN ENCODED BY GENE NO: 39

This gene is expressed in Ovarian Tumor 10-3-95.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of reproductive system disorders; particularly male and female infertility, placental and uterine disorders (e.g. endometriosis), and cancer of reproductive organs (e.g. testicular and ovarian cancer). See "Reproductive System Disorders" section, infra. The tissue distribution also indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of cancer and other hyperproliferative disorders (e.g., see "Hyperproliferative Disorders" section, infra).

FEATURES OF PROTEIN ENCODED BY GENE NO: 40

The computer algorithm BLASTX has been used to determine that the translation product of this gene shares sequence homology with, as a non-limiting example, the sequence accessible through the following database accession no. sp|BAB01630|BAB01630 (all information available through the recited accession number is incorporated herein by reference). Based on the structural similarity these homologous polypeptides are expected to share at least some biological activities. Such activities are known in the art, some of which are described elsewhere herein. Assays for determining such activities are also known in the art, some of which have been described elsewhere herein. Preferred polypeptides of the invention comprise a polypeptide having the amino acid sequence set out in the sequence listing as SEQ ID NO:411.

This gene is expressed in PC3 Prostate cell line.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of reproductive system disorders; particularly male and female infertility, placental and uterine disorders (e.g. endometriosis), and cancer of reproductive organs (e.g. testicular and ovarian cancer). See "Reproductive System Disorders" section, infra.

FEATURES OF PROTEIN ENCODED BY GENE NO: 41

Preferred polypeptides of the invention comprise a polypeptide having the amino acid sequence set out in the sequence listing as SEQ ID NO: 412 and/or SEQ ID NO: 413.

This gene is expressed in the following tissues/cDNA libraries: TF-1 Cell Line GM-CSF Treated; 12 Week Early Stage Human II, Reexcision; Soares_placenta_8to9weeks_2NbHP8to9W; Soares fetal liver spleen 1NFLS.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of immune system disorders; particularly immune cell proliferative disorders (e.g. leukemia), autoimmune disorders, and immunodeficiencies (including immunodeficiencies caused by genetic factors, microbial pathogens (e.g. HIV), chemotherapy, and radiation). See "Immune Activity" section, infra.

The tissue distribution also indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of cancer and other hyperproliferative disorders (e.g., see "Hyperproliferative Disorders" section, infra).

FEATURES OF PROTEIN ENCODED BY GENE NO: 42

The computer algorithm BLASTX has been used to determine that the translation product of this gene shares sequence homology with, as a non-limiting example, the sequence accessible through the following database accession no. sp|BAA91205|BAA91205 (all information available through the recited accession number is incorporated herein by reference) which is described therein as "CDNA

FLJ20489 FIS, CLONE KAT08285."Based on the structural similarity these homologous polypeptides are expected to share at least some biological activities. Such activities are known in the art, some of which are described elsewhere herein. Assays for determining such activities are also known in the art, some of which have been described elsewhere herein. Preferred polypeptides of the invention comprise a polypeptide having the amino acid sequence set out in the sequence listing as SEQ ID NO: 414.

This gene is expressed in the following tissues/cDNA libraries: Primary Dendritic Cells, lib 1 and to a lesser extent in Rectum normal; Human Thymus; Healing groin wound, 7.5 hours post incision; Jurkat cells, thiouridine activated, fract II; NK CellsYao20 IL2 treated for 48 hrs; NCI_CGAP_Ov23; Adenocarcinoma of Ovary, Human Cell Line, # OVCAR-3; Human pancreatic islet; Human Pre-Differentiated Adipocytes; Breast, Cancer: (4004943 A5); Healing groin wound - zero hr post-incision (control); NCI_CGAP_CLL1; Macrophage (GM-CSF treated); Myoloid Progenitor Cell Line; B-cells (stimulated); NCI_CGAP_Kid3; Dendritic cells, pooled; H. Frontal cortex,epileptic,re-excision; NTERA2 teratocarcinoma cell line+retinoic acid (14 days); normalized infant brain cDNA; T cell helper II; Soares_pregnant_uterus_NbHPU; NCI_CGAP_GCB1 and NCI_CGAP_Sub5.

FEATURES OF PROTEIN ENCODED BY GENE NO: 43

Preferred polypeptides of the invention comprise a polypeptide having the amino acid sequence set out in the sequence listing as SEQ ID NO:415, SEQ ID NO: 416 and/or SEQ ID NO:417.

This gene is expressed in the following tissues/cDNA libraries: Skin, burned; CD34 depleted Buffy Coat (Cord Blood).

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of wound healing and disorders of epithelial cell proliferation; particularly chronically open wounds, skin grafting, and cancers of epithelial tissues (e.g. lung and colon cancer). See "Wound Healing and Epithelial Cell Proliferation" section, infra.

FEATURES OF PROTEIN ENCODED BY GENE NO: 44

The computer algorithm BLASTX has been used to determine that the translation product of this gene shares sequence homology with, as a non-limiting example, the sequence accessible through the following database accession no. pir|T08708|T08708 (all information available through the recited accession number is incorporated herein by reference). Preferred polypeptides of the invention comprise a polypeptide having the amino acid sequence set out in the sequence listing as SEQ ID NO: 418 .

This gene is expressed in the following tissues/cDNA libraries: Soares_testis_NHT and to a lesser extent in NCI_CGAP_Ut1; Soares_fetal_liver_spleen_1NFLS_S1; Soares_NFL_T_GBC_S1; NCI_CGAP_Pr10; Human Fetal Kidney, Reexcision; Soares_fetal_lung_NbHL19W; Soares_total_fetus_Nb2HF8_9w; Soares_pregnant_uterus_NbHPU; Soares infant brain 1NIB; NCI_CGAP_Ut4; NCI_CGAP_Br2; Soares breast 2NbHBst; NCI_CGAP_Kid11; NCI_CGAP_Kid5; NCI_CGAP_Brn23; Soares_multiple_sclerosis_2NbHMSP; NCI_CGAP_Lu5; Colon Tumor II; Soares_fetal_heart_NbHH19W; Human adult lung 3' directed MboI cDNA; Jurkat Cells; NCI_CGAP_Kid12; Human White Adipose; NCI_CGAP_Lu24; NCI_CGAP_Ut3; Human Tonsils, Lib 2; NCI_CGAP_Co10; NCI_CGAP_Lym12; NCI_CGAP_Alv1; NCI_CGAP_Ut2; H. Lymph node breast Cancer; Breast, Normal: (4005522B2); H. Epididiymus, caput & corpus; Human Umbilical Vein, Reexcision; H. Epididiymus, cauda; NCI_CGAP_Pr28; NCI_CGAP_Gas4; Human Uterine Cancer; Palate normal; Fetal Heart; Soares breast 3NbHBst; NCI_CGAP_GC4; Adipocytes; Human Synovial Sarcoma; Human Ovarian Cancer Reexcision; Endothelial cells-control; NCI_CGAP_Brn25; Pancreas Islet Cell Tumor; Soares_senescent_fibroblasts_NbHSF; NCI_CGAP_Kid3; Prostate Adenocarcinoma; Soares ovary tumor NbHOT; NTERA2 teratocarcinoma cell line+retinoic acid (14 days); Nine Week Old Early Stage Human; NCI_CGAP_GCB1; Soares fetal liver spleen 1NFLS and NCI_CGAP_Br18.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of reproductive system

disorders; particularly male and female infertility, placental and uterine disorders (e.g. endometriosis), and cancer of reproductive organs (e.g. testicular and ovarian cancer). See "Reproductive System Disorders" section, infra.

The tissue distribution also indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of cancer and other hyperproliferative disorders (e.g., see "Hyperproliferative Disorders" section, infra).

FEATURES OF PROTEIN ENCODED BY GENE NO: 45

The computer algorithm BLASTX has been used to determine that the translation product of this gene shares sequence homology with, as a non-limiting example, the sequence accessible through the following database accession no. sp|P70222|P70222 (all information available through the recited accession number is incorporated herein by reference). Based on the structural similarity these homologous polypeptides are expected to share at least some biological activities. Such activities are known in the art, some of which are described elsewhere herein. Assays for determining such activities are also known in the art, some of which have been described elsewhere herein. Preferred polypeptides of the invention comprise a polypeptide having the amino acid sequence set out in the sequence listing as SEQ ID NO: 419, SEQ ID NO: 420 and/or SEQ ID NO:421.

This gene is expressed in the following tissues/cDNA libraries: Human adult small intestine,re-excision; Ovarian Tumor 10-3-95; Stomach Normal; Human Placenta; NTERA2, control; Endothelial-induced; Human Bone Marrow, treated; PC3 Prostate cell line.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of gastrointestinal system disorders; particularly inflammatory diseases (e.g. gastroenteritis and stomach ulcers) and gastrointestinal cancers (e.g. stomach and colon cancer. See "Gastrointestinal Disorders" section, infra. The tissue distribution also indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of cancer

and other hyperproliferative disorders (e.g., see "Hyperproliferative Disorders" section, infra).

FEATURES OF PROTEIN ENCODED BY GENE NO: 46

The computer algorithm BLASTX has been used to determine that the translation product of this gene shares sequence homology with, as a non-limiting example, the sequence accessible through the following database accession no. sp|Q90806|Q90806 (all information available through the recited accession number is incorporated herein by reference) which is described therein as "OLFACTORY RECEPTOR 2 (FRAGMENT)." Based on the structural similarity these homologous polypeptides are expected to share at least some biological activities. Such activities are known in the art, some of which are described elsewhere herein. Assays for determining such activities are also known in the art, some of which have been described elsewhere herein. Preferred polypeptides of the invention comprise a polypeptide having the amino acid sequence set out in the sequence listing as SEQ ID NO:422.

This gene is expressed in Human Testes, Reexcision.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of reproductive system disorders; particularly male and female infertility, placental and uterine disorders (e.g. endometriosis), and cancer of reproductive organs (e.g. testicular and ovarian cancer). See "Reproductive System Disorders" section, infra.

FEATURES OF PROTEIN ENCODED BY GENE NO: 47

This gene is expressed in the following tissues/cDNA libraries: NCI_CGAP_Co8 and to a lesser extent in Colon Normal III; NCI_CGAP_Co3; Human Colon, re-excision; Normal colon; Soares ovary tumor NbHOT; NCI_CGAP_Lu19; NCI_CGAP_Kid12; Rectum tumour; NCI_CGAP_Sub3; Keratinocyte, lib 3; Human Colon, differential expression; Human colorectal cancer; NCI_CGAP_Ut3; NCI_CGAP_Co9; Ovarian cancer, Serous Papillary Adenocarcinoma; Prostate BPH; Healing groin wound, 7.5 hours post incision; Liver

Tumour Met 5 Tu; Palate normal; Colon, normal; NCI_CGAP_Kid11 and Colon Normal II.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of gastrointestinal system disorders; particularly inflammatory diseases (e.g. gastroenteritis and stomach ulcers) and gastrointestinal cancers (e.g. stomach and colon cancer. See "Gastrointestinal Disorders" section, infra. The tissue distribution also indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of cancer and other hyperproliferative disorders (e.g., see "Hyperproliferative Disorders" section, infra).

FEATURES OF PROTEIN ENCODED BY GENE NO: 48

The computer algorithm BLASTX has been used to determine that the translation product of this gene shares sequence homology with, as a non-limiting example, the sequence accessible through the following Genbank database accession no. sp|O95413|O95413 (all information available through the recited accession number is incorporated herein by reference) which is described therein as "SIALOMUCIN CD164." Based on the structural similarity these homologous polypeptides are expected to share at least some biological activities. Such activities are known in the art, some of which are described elsewhere herein. Assays for determining such activities are also known in the art, some of which have been described elsewhere herein. Preferred polypeptides of the invention comprise a polypeptide having the amino acid sequence set out in the sequence listing as SEQ ID NO: 423 .

This gene is expressed in Chondrocytes.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of skeletomuscular system disorders and abnormalities; particularly rheumatoid arthritis and cartilage regeneration.

FEATURES OF PROTEIN ENCODED BY GENE NO: 49

The computer algorithm BLASTX has been used to determine that the translation product of this gene shares sequence homology with, as a non-limiting example, the sequence accessible through the following database accession no. sp|Q9VTS0|Q9VTS0 (all information available through the recited accession number is incorporated herein by reference) which is described therein as "CG6938 PROTEIN." Based on the structural similarity these homologous polypeptides are expected to share at least some biological activities. Such activities are known in the art, some of which are described elsewhere herein. Assays for determining such activities are also known in the art, some of which have been described elsewhere herein. Preferred polypeptides of the invention comprise a polypeptide having the amino acid sequence set out in the sequence listing as SEQ ID NO: <SEQIDNO:424 .

This gene is expressed in the following tissues/cDNA libraries: Colon Normal III and to a lesser extent in Healing Abdomen wound,70&90 min post incision; CD40 activated monocyte dendritic cells; Ulcerative Colitis; Ovarian Tumor 10-3-95 and Rejected Kidney, lib 4.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of gastrointestinal system disorders; particularly inflammatory diseases (e.g. gastroenteritis and stomach ulcers) and gastrointestinal cancers (e.g. stomach and colon cancer. See "Gastrointestinal Disorders" section, infra.

FEATURES OF PROTEIN ENCODED BY GENE NO: 50

Preferred polypeptides of the invention comprise a polypeptide having the amino acid sequence set out in the sequence listing as SEQ ID NO:425, SEQ ID NO:426 and/or SEQ ID NO:427.

This gene is expressed in the following tissues/cDNA libraries: NCI_CGAP_Ut1; Human Activated T-Cells; Human Neutrophil, Activated; Soares ovary tumor NbHOT.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of immune system disorders; particularly immune cell proliferative disorders (e.g. leukemia), autoimmune disorders, and immunodeficiencies (including immunodeficiencies caused by genetic factors, microbial pathogens (e.g. HIV), chemotherapy, and radiation). See "Immune Activity" section, infra.

FEATURES OF PROTEIN ENCODED BY GENE NO: 51

The computer algorithm BLASTX has been used to determine that the translation product of this gene shares sequence homology with, as a non-limiting example, the sequence accessible through the following Genbank database accession no. sp|Q9UHT1|Q9UHT1 (all information available through the recited accession number is incorporated herein by reference) which is described therein as "PRO1902". Based on the structural similarity these homologous polypeptides are expected to share at least some biological activities. Such activities are known in the art, some of which are described elsewhere herein. Assays for determining such activities are also known in the art, some of which have been described elsewhere herein. Preferred polypeptides of the invention comprise a polypeptide having the amino acid sequence set out in the sequence listing as SEQ ID NO: 428 and/or SEQ ID NO: 429 .

This gene is expressed in the following tissues/cDNA libraries: H. cerebellum, Enzyme subtracted; Human Whole Brain, re-excision; NCI_CGAP_Lu5.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of neurological disorders; particularly brain cancer and neurodegenerative disorders (such as Alzheimer's, Parkinson's and Huntington's Disease). See "Neural Activity and Neurological Diseases" section, infra.

FEATURES OF PROTEIN ENCODED BY GENE NO: 52

This gene is expressed in the following tissues/cDNA libraries: Soares_fetal_heart_NbHH19W and to a lesser extent in NCI_CGAP_CLL1; Human Cerebellum; Colon Tumor II; Colon Normal III; Stratagene hNT neuron (#937233); Soares_parathyroid_tumor_NbHPA; 1-NIB; NCI_CGAP_Brn52; NCI_CGAP_Co1; NCI_CGAP_Lu24; NCI_CGAP_Ut4; NCI_CGAP_Ut3; Patient #6 Acute Myeloid Leukemia/SGAH; Stratagene fetal spleen (#937205); Palate carcinoma; NCI_CGAP_Kid11; T-Cell PHA 24 hrs; Corpus Callosum; NCI_CGAP_Lu19; Whole 6 Week Old Embryo; Lung, Normal: (4005313 B1); Human (Caco-2) cell line, adenocarcinoma, colon, remake; NCI_CGAP_Co11; Human (HCC) cell line liver (mouse) metastasis, remake; NCI_CGAP_Kid8; Human Cerebellum, subtracted; Lung, Cancer (4005313 A3): Invasive Poorly Differentiated Lung Adenocarcinoma,; Human adult (K.Okubo); Breast, Cancer: (4005522 A2); Human Osteoclastoma Stromal Cells - unamplified; B Cell lymphoma; NCI_CGAP_Co14; Human Amygdala,re-excision; wilm's tumor; Human Infant Brain; NCI_CGAP_Gas4; Human Chondrosarcoma; Soares adult brain N2b5HB55Y; NCI_CGAP_Pan1; Colon Normal II; Human Synovial Sarcoma; Bone marrow; NCI_CGAP_GC6; Pancreas Islet Cell Tumor; Soares_senescent_fibroblasts_NbHSF; NCI_CGAP_Kid5; T Cell helper I; Resting T-Cell Library,II; Soares melanocyte 2NbHM; Keratinocyte; Nine Week Old Early Stage Human; Activated T-cell(12h)/Thiouridine-re-excision; NCI_CGAP_GCB1; Primary Dendritic Cells, lib 1 and NCI_CGAP_GU1.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of cardiovascular disorders; particularly heart disease, high blood pressure, cardiac ischemia, and coronary artery disease. See "Cardiovascular Disorders" section, infra. The tissue distribution also indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of cancer and other hyperproliferative disorders (e.g., see "Hyperproliferative Disorders" section, infra).

FEATURES OF PROTEIN ENCODED BY GENE NO: 53

The computer algorithm BLASTX has been used to determine that the translation product of this gene shares sequence homology with, as a non-limiting example, the sequence accessible through the following database accession no. sp|CAC00650|CAC00650 (all information available through the recited accession number is incorporated herein by reference) which is described therein as "ER protein 58." Based on the structural similarity these homologous polypeptides are expected to share at least some biological activities. Such activities are known in the art, some of which are described elsewhere herein. Assays for determining such activities are also known in the art, some of which have been described elsewhere herein. Preferred polypeptides of the invention comprise a polypeptide having the amino acid sequence set out in the sequence listing as SEQ ID NO:430 and/or SEQ ID NO:431.

This gene is expressed in the following tissues/cDNA libraries: Soares fetal liver spleen 1NFLS and to a lesser extent in Stratagene HeLa cell s3 937216; NTERA2 + retinoic acid, 14 days; NCI_CGAP_Kid11; CAMA1Ee Cell Line; NCI_CGAP_Kid12; NCI_CGAP_Lu24; Human OB HOS treated (10 nM E2) fraction I; Lung, Cancer (4005163 B7): Invasive, Poorly Diff. Adenocarcinoma, Metastatic; Human Osteoclastoma, re-excision; Human Chronic Synovitis; Stratagene lung carcinoma 937218; Gessler Wilms tumor; TNFR degenerate oligo; 12 Week Old Early Stage Human, II; Ovary, Cancer: (15799A1F) Poorly differentiated carcinoma; NCI_CGAP_GC4; NCI_CGAP_GC6; Human Osteoclastoma; Human Fetal Heart; Human Thymus Stromal Cells; NTERA2 teratocarcinoma cell line+retinoic acid (14 days); Human Endometrial Tumor; Human 8 Week Whole Embryo; Soares_fetal_lung_NbHL19W; Colon Tumor II; Soares_fetal_liver_spleen_1NFLS_S1 and Soares_NhHMPu_S1.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene would be useful for the diagnosis, prevention, and or treatment of liver disorders and cancers. For example, the protein can be used for the detection, treatment, and/or prevention of Wilson's disease, cirrhosis, fibrosis, bilirubin metabolism, hepatomegaly, cholestasis, liver cancer (for example, hepatoblastoma), jaundice, hepatitis (acuta and chronic) and liver metabolic diseases and conditions attributable to the differentiation of hepatocyte progenitor cells. The tissue distribution also indicates polynucleotides and polypeptides corresponding to

this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of cancer and other hyperproliferative disorders (e.g., see "Hyperproliferative Disorders" section, infra).

FEATURES OF PROTEIN ENCODED BY GENE NO: 54

This gene is expressed in the following tissues/cDNA libraries: Human Activated T-Cells, re-excision and to a lesser extent in NCI_CGAP_Brn35; Human Hypothalamus,schizophrenia, re-excision; Human Testes Tumor, re-excision and Activated T-cell(12h)/Thiouridine-re-excision.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of immune system disorders; particularly immune cell proliferative disorders (e.g. leukemia), autoimmune disorders, and immunodeficiencies (including immunodeficiencies caused by genetic factors, microbial pathogens (e.g. HIV), chemotherapy, and radiation). See "Immune Activity" section, infra.

FEATURES OF PROTEIN ENCODED BY GENE NO: 55

This gene is expressed in the following tissues/cDNA libraries: Human Endometrial Tumor and to a lesser extent in Human Activated T-Cells, re-excision; Spleen, Chronic lymphocytic leukemia; Bone Marrow Cell Line (RS4,11); H. Leukocytes, control; Jurkat Cells; Human B Cell 8866; Amniotic Cells - Primary Culture; Ovarian Cancer; Human Thymus; HUMAN JURKAT MEMBRANE BOUND POLYSOMES; Human Activated Monocytes; Healing groin wound, 7.5 hours post incision; breast lymph node CDNA library; Early Stage Human Brain; CHME Cell Line,treated 5 hrs; Normal colon; Primary Dendritic cells,frac 2; Anergic T-cell; Human Fetal Heart; Endothelial cells-control; human tonsils; Human Microvascular Endothelial Cells, fract. A; Human Placenta; Monocyte activated; T-Cell PHA 24 hrs and Human Cerebellum.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of reproductive system

disorders; particularly male and female infertility, placental and uterine disorders (e.g. endometriosis), and cancer of reproductive organs (e.g. testicular and ovarian cancer). See "Reproductive System Disorders" section, infra. The tissue distribution also indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of immune system disorders; particularly immune cell proliferative disorders (e.g. leukemia), autoimmune disorders, and immunodeficiencies (including immunodeficiencies caused by genetic factors, microbial pathogens (e.g. HIV), chemotherapy, and radiation). See "Immune Activity" section, infra.

FEATURES OF PROTEIN ENCODED BY GENE NO: 56

This gene is expressed in the following tissues/cDNA libraries: NCI_CGAP_GCB1 and to a lesser extent in NCI_CGAP_Brn25; Human Neutrophil, Activated; Soares_senescent_fibroblasts_NbHSF; Soares_testis_NHT; NCI_CGAP_CLL1; Spleen, Chronic lymphocytic leukemia; Soares_parathyroid_tumor_NbHPA; Soares_pregnant_uterus_NbHPU; Neuroblastoma; Soares breast 2NbHBst; Soares_fetal_lung_NbHL19W; Soares placenta Nb2HP; NCI_CGAP_Brn53; Human Umbilical Vein, Endo. remake; CD34 depleted Buffy Coat (Cord Blood); NCI_CGAP_Pr22; Stratagene pancreas (#937208); CHME Cell Line,untreated; CHME Cell Line,treated 5 hrs; Human Fetal Lung III; CD34 depleted Buffy Coat (Cord Blood), re-excision; NCI_CGAP_Kid3; neutrophils control; Soares_fetal_heart_NbHH19W; Soares fetal liver spleen 1NFLS; b4HB3MA-FT20%-Biotin; Activated T-Cells, 8 hrs, subtracted; NCI_CGAP_GCB0; Human epithelioid sarcoma; Normal Human Trabecular Bone Cells; Human Neutrophils, Activated, re-excision; NCI_CGAP_Ut4; Adenocarcinoma of Ovary, Human Cell Line; Stratagene placenta (#937225); Smooth muscle, IL1b induced; Amniotic Cells - Primary Culture; NCI_CGAP_Co10; NCI_CGAP_Co14; NCI_CGAP_Lym12; Jurkat T-cell G1 phase; NCI_CGAP_Pr28; NCI_CGAP_Gas4; Human Activated Monocytes; Human Thymus; Human Whole Six Week Old Embryo; Human Testes Tumor, re-excision; Human adult testis, large inserts; Ovarian Tumor 10-3-95; breast lymph node CDNA library; Human Substantia Nigra; Ovary, Cancer (9809C332): Poorly differentiated adenocarcinoma; Human Synovial

Sarcoma; Neutrophils control, re-excision; T-Cell PHA 16 hrs; NTERA2, control; Endothelial-induced; Activated T-Cell (12hs)/Thiouridine labelledEco; B-cells (stimulated); NCI_CGAP_Kid5; NCI_CGAP_Brn23; Human Placenta; Human Bone Marrow, treated; Soares ovary tumor NbHOT; Dendritic cells, pooled; NTERA2 teratocarcinoma cell line+retinoic acid (14 days); Hodgkin's Lymphoma II; T cell helper II; Soares infant brain 1NIB; NCI_CGAP_Lu28 and NCI_CGAP_Sub6.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of immune system disorders; particularly immune cell proliferative disorders (e.g. leukemia), autoimmune disorders, and immunodeficiencies (including immunodeficiencies caused by genetic factors, microbial pathogens (e.g. HIV), chemotherapy, and radiation). See "Immune Activity" section, infra. The tissue distribution also indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of neurological disorders; particularly brain cancer and neurodegenerative disorders (such as Alzheimer's, Parkinson's and Huntington's Disease). See "Neural Activity and Neurological Diseases" section, infra.

FEATURES OF PROTEIN ENCODED BY GENE NO: 57

This gene is expressed in Neutrophils IL-1 and LPS induced.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of immune system disorders; particularly immune cell proliferative disorders (e.g. leukemia), autoimmune disorders, and immunodeficiencies (including immunodeficiencies caused by genetic factors, microbial pathogens (e.g. HIV), chemotherapy, and radiation). See "Immune Activity" section, infra.

FEATURES OF PROTEIN ENCODED BY GENE NO: 58

The computer algorithm BLASTX has been used to determine that the translation product of this gene shares sequence homology with, as a non-limiting

example, the sequence accessible through the following database accession no. pir|T33123|T33123 (all information available through the recited accession number is incorporated herein by reference). Based on the structural similarity these homologous polypeptides are expected to share at least some biological activities. Such activities are known in the art, some of which are described elsewhere herein. Assays for determining such activities are also known in the art, some of which have been described elsewhere herein. Preferred polypeptides of the invention comprise a polypeptide having the amino acid sequence set out in the sequence listing as SEQ ID NO: 432.

This gene is expressed in the following tissues/cDNA libraries: Soares_testis_NHT and to a lesser extent in Soares_fetal_heart_NbHH19W; Soares breast 3NbHBst; Colon Normal III; Soares infant brain 1NIB; Pancreas Islet Cell Tumor; NCI_CGAP_GCB1; Soares_fetal_lung_NbHL19W; Hepatocellular Tumor, re-excision; NCI_CGAP_Kid5; NCI_CGAP_Brn23; Soares fetal liver spleen 1NFLS; NCI_CGAP_Co14; NCI_CGAP_Ut1; NCI_CGAP_Brn25; Soares_parathyroid_tumor_NbHPA; Hepatocellular Tumor,re-excision; NCI_CGAP_Pr3; NCI_CGAP_Pan1; Soares_placenta_8to9weeks_2NbHP8to9W; Human Thymus Stromal Cells; Human Fetal Kidney; NCI_CGAP_Co3; Human Liver, normal; Early Stage Human Brain; Human Endometrial Tumor; Colon Tumor II; Soares_total_fetus_Nb2HF8_9w; Primary Dendritic Cells, lib 1; Smooth Muscle Serum Treated, Norm; NCI_CGAP_Ut4; NCI_CGAP_Ut3; human corpus colosum; Human normal ovary(#9610G215); H. Kidney Cortex, subtracted; Human endometrial stromal cells; Colon Normal; Human Umbilical Vein Endothelial Cells, uninduced; Stratagene HeLa cell s3 937216; CHME Cell Line,untreated; Palate carcinoma; Human Fetal Kidney, Reexcision; Normal colon; Endothelial-induced; B-cells (stimulated); Human Adult Pulmonary,re-excision; NCI_CGAP_Kid3; Monocyte activated; Soares ovary tumor NbHOT; NCI_CGAP_Lu5; PC3 Prostate cell line; Hodgkin's Lymphoma II; Soares placenta Nb2HP; Soares_NhHMPu_S1; Human Striatum Depression, re-rescue; NCI_CGAP_Lu19; NCI_CGAP_Kid12; HL-60, RA 4h, Subtracted; NCI_CGAP_Kid8; NCI_CGAP_Ov23; Stratagene neuroepithelium NT2RAMI 937234; Human Primary Breast Cancer; STRATAGENE Human skeletal muscle cDNA library, cat. #936215.; Hepatocellular Tumor; B Cell

lymphoma; Stratagene ovary (#937217); Human Whole Brain #2 - Oligo dT > 1.5Kb; NCI_CGAP_Lym12; Synovial hypoxia; LNCAP prostate cell line; Human Chronic Synovitis; Human Adult Small Intestine; Stratagene lung carcinoma 937218; Stratagene neuroepithelium (#937231); H. Epididiymus, caput & corpus; Human Bone Marrow, re-excision; NCI_CGAP_Kid6; Human Prostate Cancer, Stage C, re-excission; Ovary, Cancer: (15799A1F) Poorly differentiated carcinoma; HUMAN JURKAT MEMBRANE BOUND POLYSOMES; NCI_CGAP_Gas4; Apoptotic T-cell; Human Hippocampus; Liver, Hepatoma; Human umbilical vein endothelial cells, IL-4 induced; Human Fetal Brain; Olfactory epithelium,nasalcavity; Human Whole Six Week Old Embryo; Stratagene liver (#937224); Fetal Liver, subtraction II; 12 Week Old Early Stage Human; NCI_CGAP_Co8; NCI_CGAP_GC4; Colon Normal II; NCI_CGAP_GC6; 12 Week Early Stage Human II, Reexcision; Primary Dendritic cells,frac 2; Human Primary Breast Cancer Reexcision; Human Adult Heart,re-excision; H. Frontal cortex,epileptic,re-excision; Keratinocyte; Activated T-cell(12h)/Thiouridine-re-excision; Soares_pregnant_uterus_NbHPU; NCI_CGAP_Sub5; NCI_CGAP_Brn53; Leukocyte and Lung, 4 screens; Human Fetal Kidney; Thyroid Thyroiditis; Human colon mucosa; 7 Week Old Early Stage Human, subtracted; Human Umbilical Vein Endothelial cells, frac B, re-excision; Prostate; H. Striatum Depression, subtracted; Human osteoarthritis,fraction I; NCI_CGAP_HN4; NCI_CGAP_Co2; NCI_CGAP_Br3; Prostate Adenocarcinoma cell line cultured in vivo in mice; Ovarian Cancer Cell Line(Xenograft) ES-2; NCI_CGAP_Pr21; HUMAN TONSILS, FRACTION 2; Human retina cDNA Tsp509I-cleaved sublibrary; Barstead spleen HPLRB2; Human Aortic Endothelium; Human colon carcinoma (HCC) cell line, remake; Human Adult Pulmonary; NCI_CGAP_Pr25; Human Colon Carcinoma (HCC) cell line; Hodgkin's Lymphoma I; HSC172 cells; Human Pituitary, subtracted; Frontal lobe,dementia,re-excision; Supt Cells, cyclohexamide treated; Human Fetal Bone; human colon cancer; Aorta endothelial cells + TNF-a; Human heart cDNA (YNakamura); Lung, Cancer (4005163 B7): Invasive, Poorly Diff. Adenocarcinoma, Metastatic; Human Quadriceps; Human Colon Cancer,re-excision; Human Tonsils, Lib 2; STROMAL -OSTEOCLASTOMA; Alzheimers, spongy change; H Female Bladder, Adult; Ku 812F Basophils Line; Human pancreatic islet; Synovial hypoxia-RSF subtracted; Human Stomach,re-

excision; Ovarian cancer, Serous Papillary Adenocarcinoma; NCI_CGAP_Co10; Ovarian Cancer, # 9702G001; Human Osteosarcoma; Colon, tumour; NCI_CGAP_Pr12; Human Adipose Tissue, re-excision; Human Pituitary, subt IX; Prostate BPH; NCI_CGAP_Ut2; Breast, Normal: (4005522B2); H. Kidney Medulla, re-excision; NCI_CGAP_Pr2; Colon Tumor; HM1; NCI_CGAP_Pr22; Breast Cancer Cell line, angiogenic; Monocyte activated, re-excision; NCI_CGAP_Pr28; Human Fetal Dura Mater; Stromal cell TF274; Human Prostate Cancer, Stage B2, re-excision; Macrophage-oxLDL; Human Hypothalmus,Schizophrenia; Soares_NSF_F8_9W_OT_PA_P_S1; Ovary, Cancer (15395A1F): Grade II Papillary Carcinoma; CD40 activated monocyte dendridic cells; Human Thymus; Hemangiopericytoma; Human Chondrosarcoma; Human Activated T-Cells, re-excision; NCI_CGAP_CLL1; Soares breast 2NbHBst; Human Adrenal Gland Tumor; Ulcerative Colitis; Smooth muscle, serum induced,re-exc; Colon Tumor; Healing groin wound, 6.5 hours post incision; Ovarian Tumor 10-3-95; Colon, normal; Rectum tumour; breast lymph node CDNA library; Human endometrial stromal cells-treated with progesterone; NCI_CGAP_Kid11; CHME Cell Line,treated 5 hrs; H Macrophage (GM-CSF treated), re-excision; Adipocytes; Ovary, Cancer (9809C332): Poorly differentiated adenocarcinoma; Ovary, Cancer(4004650 A3): Well-Differentiated Micropapillary Serous Carcinoma; Human Synovial Sarcoma; Human Placenta; Pancreas normal PCA4 No; Human Fetal Lung III; T-Cell PHA 16 hrs; NTERA2, control; Myoloid Progenitor Cell Line; Activated T-Cell (12hs)/Thiouridine labelledEco; Human Amygdala; Soares_senescent_fibroblasts_NbHSF; Soares_multiple_sclerosis_2NbHMSP; Smooth muscle,control; Prostate Adenocarcinoma; Pancreas Tumor PCA4 Tu; Spleen, Chronic lymphocytic leukemia; NTERA2 teratocarcinoma cell line+retinoic acid (14 days); Osteoblasts; Soares melanocyte 2NbHM; Nine Week Old Early Stage Human; Human Cerebellum; Soares_NFL_T_GBC_S1; NCI_CGAP_GU1; NCI_CGAP_Co17; NCI_CGAP_Sar4; NCI_CGAP_Sub4 and NCI_CGAP_Kid13.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of reproductive system disorders; particularly male and female infertility, placental and uterine disorders (e.g.

endometriosis), and cancer of reproductive organs (e.g. testicular and ovarian cancer). See "Reproductive System Disorders" section, infra. The tissue distribution also indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of cancer and other hyperproliferative disorders (e.g., see "Hyperproliferative Disorders" section, infra).

FEATURES OF PROTEIN ENCODED BY GENE NO: 59

The computer algorithm BLASTX has been used to determine that the translation product of this gene shares sequence homology with, as a non-limiting example, the sequence accessible through the following database accession no. sp|AAF31162|AAF31162 (all information available through the recited accession number is incorporated herein by reference) which is described therein as "Erythroid membrane-associated protein ERMAP." Based on the structural similarity these homologous polypeptides are expected to share at least some biological activities. Such activities are known in the art, some of which are described elsewhere herein. Assays for determining such activities are also known in the art, some of which have been described elsewhere herein. Preferred polypeptides of the invention comprise a polypeptide having the amino acid sequence set out in the sequence listing as SEQ ID NO:433.

This gene is expressed in neural/sensory, reproductive, immune/hematopoietic tissues.

The protein homology indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of hematopoietic disorders; particularly anemias, clotting disorders/abnormalities (e.g. hemophilia, myocardial infarction, stroke), and leukemia. See "Blood Related Disorders" section, infra. Also, for disorders in neural and reproductive systems. The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of cancer and other hyperproliferative disorders (e.g., see "Hyperproliferative Disorders" section, infra).

FEATURES OF PROTEIN ENCODED BY GENE NO: 60

This gene is expressed in the following tissues/cDNA libraries: NTERA2 teratocarcinoma cell line + retinoic acid (14 days); Activated T-cell(12h)/Thiouridine-re-excision.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of cancer and other hyperproliferative disorders (e.g., see "Hyperproliferative Disorders" section, infra). The tissue distribution also indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of immune system disorders; particularly immune cell proliferative disorders (e.g. leukemia), autoimmune disorders, and immunodeficiencies (including immunodeficiencies caused by genetic factors, microbial pathogens (e.g. HIV), chemotherapy, and radiation). See "Immune Activity" section, infra.

FEATURES OF PROTEIN ENCODED BY GENE NO: 61

This gene is expressed in the following tissues/cDNA libraries: NCI_CGAP_GC6; Soares infant brain 1NIB and to a lesser extent in Colon Normal II; T-Cell PHA 16 hrs; Monocyte activated; Spleen, Chronic lymphocytic leukemia and Soares_NFL_T_GBC_S1.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of neurological disorders; particularly brain cancer and neurodegenerative disorders (such as Alzheimer's, Parkinson's and Huntington's Disease). See "Neural Activity and Neurological Diseases" section, infra. The tissue distribution also indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of immune system disorders; particularly immune cell proliferative disorders (e.g. leukemia), autoimmune disorders, and immunodeficiencies (including

immunodeficiencies caused by genetic factors, microbial pathogens (e.g. HIV), chemotherapy, and radiation). See "Immune Activity" section, infra.

FEATURES OF PROTEIN ENCODED BY GENE NO: 62

The computer algorithm BLASTX has been used to determine that the translation product of this gene shares sequence homology with, as a non-limiting example, the sequence accessible through the following database accession no. sp|O95070|O95070 (all information available through the recited accession number is incorporated herein by reference) which is described therein as "54TMP". Based on the structural similarity these homologous polypeptides are expected to share at least some biological activities. Such activities are known in the art, some of which are described elsewhere herein. Assays for determining such activities are also known in the art, some of which have been described elsewhere herein. Preferred polypeptides of the invention comprise a polypeptide having the amino acid sequence set out in the sequence listing as SEQ ID NO:434.

This gene is expressed in Myoloid Progenitor Cell Line.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of immune system disorders; particularly immune cell proliferative disorders (e.g. leukemia), autoimmune disorders, and immunodeficiencies (including immunodeficiencies caused by genetic factors, microbial pathogens (e.g. HIV), chemotherapy, and radiation). See "Immune Activity" section, infra.

FEATURES OF PROTEIN ENCODED BY GENE NO: 63

The computer algorithm BLASTX has been used to determine that the translation product of this gene shares sequence homology with, as a non-limiting example, the sequence accessible through the following database accession no. sp|AAF75771|AAF75771 (all information available through the recited accession number is incorporated herein by reference). Based on the structural similarity these homologous polypeptides are expected to share at least some biological activities. Such activities are known in the art, some of which are described elsewhere herein.

Assays for determining such activities are also known in the art, some of which have been described elsewhere herein. Preferred polypeptides of the invention comprise a polypeptide having the amino acid sequence set out in the sequence listing as SEQ ID NO: 435 .

This gene is expressed in digestive neural/sensory, musculoskeletal, immune/hematopoietic tissues/cDNA libraries, and expressed also in endocrine, reproductive system to a less extent.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of gastrointestinal system disorders; particularly inflammatory diseases (e.g. gastroenteritis and stomach ulcers) and gastrointestinal cancers (e.g. stomach and colon cancer. See "Gastrointestinal Disorders" section, infra. Also, disorders in neural systems and musculoskeletal and immune systems.

FEATURES OF PROTEIN ENCODED BY GENE NO: 64

This gene is expressed in the following tissues/cDNA libraries: Colon Tumor II; Soares_pregnant_uterus_NbHPU; Soares_fetal_heart_NbHH19W and to a lesser extent in Stratagene endothelial cell 937223; Hodgkin's Lymphoma II; Soares_NhHMPu_S1; Human Umbilical Vein, Endo. remake; Human Umbilical Vein Endothelial Cells, uninduced; Human umbilical vein endothelial cells, IL-4 induced; NCI_CGAP_Kid11; Human Pancreas Tumor, Reexcision; NCI_CGAP_Brn25; Stratagene lung (#937210); Human Adult Heart,re-excision; Human 8 Week Whole Embryo; Soares infant brain 1NIB; Soares fetal liver spleen 1NFLS; Human Lung; NCI_CGAP_Co14; Human Prostate; Stratagene muscle 937209; Human Umbilical Vein, Reexcision; Human Prostate Cancer, Stage C, re-excission; Human Placenta (re-excision); Soares breast 3NbHBst; Human Adult Pulmonary,re-excision; NCI_CGAP_Brn23; Soares_parathyroid_tumor_NbHPA; Soares_fetal_liver_spleen_1NFLS_S1; NCI_CGAP_Sub3; Human colon cancer, metaticized to liver, subtraction; Human adult lung 3' directed MboI cDNA; Human Fetal Liver, subtracted; H Umbilical Vein Endothelial Cells, frac A, re-excision; Human White Adipose; Human Umbilical Vein Endothelial Cells, fract. A; Lung,

Cancer (4005163 B7): Invasive, Poorly Diff. Adenocarcinoma, Metastatic; Ovarian cancer, Serous Papillary Adenocarcinoma; Ovarian Cancer; Breast, Cancer: (4004943 A5); Brain Frontal Cortex, re-excision; Colon Tumor; NCI_CGAP_Ut1; Stratagene fetal spleen (#937205); NCI_CGAP_Pr28; Human Pancreas Tumor; Liver, Hepatoma; Soares_NSF_F8_9W_OT_PA_P_S1; Ovary, Cancer (15395A1F): Grade II Papillary Carcinoma; CD40 activated monocyte dendridic cells; Ulcerative Colitis; Stratagene liver (#937224); NCI_CGAP_Pan1; Human Testes Tumor, re-excision; Ovary, Cancer: (4004576 A8); Palate normal; NCI_CGAP_GC4; Bone marrow; Human Neutrophil, Activated; Human Fetal Heart; NCI_CGAP_Kid5; Human Microvascular Endothelial Cells, fract. A and Nine Week Old Early Stage Human.

When tested against K562 leukemia cell lines, supernatants removed from cells containing this gene activated the ISRE assay. Thus, it is likely that this gene activates leukemia cells through the Jak-STAT signal transduction pathway. The interferon-sensitive response element is apromoter element found upstream of many genes which are involved in the Jak-STAT pathway. The Jak-STAT pathway is a large, signal transduction pathway involved in the differentiation and proliferation of cells. Therefore, activation of the Jak-STAT pathway, reflected by the binding of the ISRE element, can be used to indicate proteins involved in the proliferation and differentiation of cells.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of gastrointestinal system disorders; particularly inflammatory diseases (e.g. gastroenteritis and stomach ulcers) and gastrointestinal cancers (e.g. stomach and colon cancer. See "Gastrointestinal Disorders" section, infra. The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of cancer and other hyperproliferative disorders (e.g., see "Hyperproliferative Disorders" section, infra).

The tissue distribution in immune cells and the fact that polypeptides of the invention activated the ISRE assay indicates the polynucleotides and polypeptides corresponding to this gene would be useful for the diagnosis and treatment of a

variety of immune system disorders. Representative uses are described in the "Immune Activity" and "Infectious Disease" sections below, in Example 11, 13, 14, 16, 18, 19, 20, and 27, and elsewhere herein. Briefly, the expression indicates a role in regulating the proliferation; survival; differentiation; and/or activation of hematopoietic cell lineages, including blood stem cells. Involvement in the regulation of cytokine production, antigen presentation, or other processes suggests a usefulness for treatment of cancer (e.g. by boosting immune responses). Expression in cells of lymphoid origin, indicates the natural gene product would be involved in immune functions. Therefore it would also be useful as an agent for immunological disorders including arthritis, asthma, immunodeficiency diseases such as AIDS, leukemia, rheumatoid arthritis, granulomatous disease, inflammatory bowel disease, sepsis, acne, neutropenia, neutrophilia, psoriasis, hypersensitivities, such as T-cell mediated cytotoxicity; immune reactions to transplanted organs and tissues, such as host-versus-graft and graft-versus-host diseases, or autoimmunity disorders, such as autoimmune infertility, lense tissue injury, demyelination, systemic lupus erythematosis, drug induced hemolytic anemia, rheumatoid arthritis, Sjogren's disease, and scleroderma. Moreover, the protein may represent a secreted factor that influences the differentiation or behavior of other blood cells, or that recruits hematopoietic cells to sites of injury. Thus, this gene product is thought to be useful in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Furthermore, the protein may also be used to determine biological activity, raise antibodies, as tissue markers, to isolate cognate ligands or receptors, to identify agents that modulate their interactions, in addition to its use as a nutritional supplement. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

FEATURES OF PROTEIN ENCODED BY GENE NO: 65

The computer algorithm BLASTX has been used to determine that the translation product of this gene shares sequence homology with, as a non-limiting example, the sequence accessible through the following Genbank database accession no. sp|BAA91131|BAA91131 (all information available through the recited accession

number is incorporated herein by reference) which is described therein as "CDNA FLJ20378 FIS, CLONE KAIA0536. Based on the structural similarity these homologous polypeptides are expected to share at least some biological activities. Such activities are known in the art, some of which are described elsewhere herein. Assays for determining such activities are also known in the art, some of which have been described elsewhere herein. Preferred polypeptides of the invention comprise a polypeptide having the amino acid sequence set out in the sequence listing as SEQ ID NO: 436 . PFAM analysis of this clone reveals a conserved motif known as HIV R-ORF/X-ORF protein signature. Genetic variation in HIV-1 and HIV-2 has been studied extensively, and the nucleotide sequences reported for several strains. ORF analysis has revealed 2 open reading frames, yielding the so-called R- and X-ORF proteins, whose functions are unknown, but which show a high degree of sequence similarity. HIVVPRVPX is a 3-element fingerprint that provides a signature for the HIV R-ORF and X-ORF proteins. The fingerprint was derived from an initial alignment of 8 sequences: the motifs were drawn from short conserved regions spanning the full alignment length.

This gene is expressed in Ovarian Cancer, # 9702G001.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of cancer and other hyperproliferative disorders (e.g., see "Hyperproliferative Disorders" section, infra). The tissue distribution also indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of reproductive system disorders; particularly male and female infertility, placental and uterine disorders (e.g. endometriosis), and cancer of reproductive organs (e.g. testicular and ovarian cancer). See "Reproductive System Disorders" section, infra.

FEATURES OF PROTEIN ENCODED BY GENE NO: 66

The computer algorithm BLASTX has been used to determine that the translation product of this gene shares sequence homology with, as a non-limiting

example, the sequence accessible through the following database accession no. pir|B64816|B64816 (all information available through the recited accession number is incorporated herein by reference) which is described therein as "ABC-type transport protein ybhF - Escherichia coli". Based on the structural similarity these homologous polypeptides are expected to share at least some biological activities. Such activities are known in the art, some of which are described elsewhere herein. Assays for determining such activities are also known in the art, some of which have been described elsewhere herein. Preferred polypeptides of the invention comprise a polypeptide having the amino acid sequence set out in the sequence listing as SEQ ID NO: 437.

This gene is expressed in the following tissues/cDNA libraries: Smooth muscle, control and to a lesser extent in Spinal cord; neutrophils control; Human Frontal Cortex, Schizophrenia; H Macrophage (GM-CSF treated), re-excision; Human Neutrophil, Activated; Human aorta polyA+ (TFujiwara); Brain Frontal Cortex, re-excision; Osteoblasts; Human Primary Breast Cancer Reexcision; Prostate BPH; Brain frontal cortex; Endothelial cells-control; Bone Cancer; Smooth muscle, control, re-excision; Stratagene placenta (#937225); Stratagene ovary (#937217); Spinal Cord, re-excision; Human Brain, Striatum; Macrophage (GM-CSF treated); Human Substantia Nigra; Neutrophils control, re-excision; Human Cardiomyopathy, subtracted; Human Neutrophils, Activated, re-excision; Human Primary Breast Cancer; Smooth Muscle- HASTE normalized; Human Whole Brain #2 - Oligo dT > 1.5Kb; Human Neutrophil; Stratagene ovarian cancer (#937219); 12 Week Old Early Stage Human, II; Stratagene HeLa cell s3 937216; 12 Week Early Stage Human II, Reexcision; Human Trachea Tumor; Human Primary Breast Cancer; Brain medulla oblongata; NCI_CGAP_Lym3; Human Prostate BPH, re-excision; NCI_CGAP_Co2; Hep G2 Cells, lambda library; NCI_CGAP_Sch1; Human colon carcinoma (HCC) cell line, remake; NCI_CGAP_Co12; Apoptotic T-cell, re-excision; Human Synovium; Human Prostate Cancer, Stage C fraction; Smooth muscle, IL1b induced; Human Adipose Tissue, re-excision; Clontech human aorta polyA+ mRNA (#6572); Apoptotic T-cell; Human Testes Tumor, re-excision; Smooth muscle, serum induced,re-exc; Human adult testis, large inserts; Human Synovial Sarcoma; Human Placenta; Endothelial-induced; Human Microvascular Endothelial Cells, fract. A;

HUMAN B CELL LYMPHOMA; H. Frontal cortex,epileptic,re-excision and Colon Normal III.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of neurological disorders; particularly brain cancer and neurodegenerative disorders (such as Alzheimer's, Parkinson's and Huntington's Disease). See "Neural Activity and Neurological Diseases" section, infra. The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of immune system disorders; particularly immune cell proliferative disorders (e.g. leukemia), autoimmune disorders, and immunodeficiencies (including immunodeficiencies caused by genetic factors, microbial pathogens (e.g. HIV), chemotherapy, and radiation). See "Immune Activity" section, infra.

FEATURES OF PROTEIN ENCODED BY GENE NO: 67

This gene is expressed in the following tissues/cDNA libraries: Prostate cancer (adenocarcinoma); Ovary, Cancer: (4004576 A8); T-Cell PHA 24 hrs.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of reproductive system disorders; particularly male and female infertility, placental and uterine disorders (e.g. endometriosis), and cancer of reproductive organs (e.g. testicular and ovarian cancer). See "Reproductive System Disorders" section, infra. The tissue distribution also indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of cancer and other hyperproliferative disorders (e.g., see "Hyperproliferative Disorders" section, infra).

FEATURES OF PROTEIN ENCODED BY GENE NO: 68

The computer algorithm BLASTX has been used to determine that the translation product of this gene shares sequence homology with, as a non-limiting example, the sequence accessible through the following database accession no. sp|BAB01630|BAB01630 (all information available through the recited accession number is incorporated herein by reference). Preferred polypeptides of the invention comprise a polypeptide having the amino acid sequence set out in the sequence listing as SEQ ID NO: 438.

This gene is expressed in Neutrophils control, re-excision.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of immune system disorders; particularly immune cell proliferative disorders (e.g. leukemia), autoimmune disorders, and immunodeficiencies (including immunodeficiencies caused by genetic factors, microbial pathogens (e.g. HIV), chemotherapy, and radiation). See "Immune Activity" section, infra.

FEATURES OF PROTEIN ENCODED BY GENE NO: 69

This gene is expressed in the following tissues/cDNA libraries: Soares infant brain 1NIB and to a lesser extent in Stratagene lung carcinoma 937218; Soares_multiple_sclerosis_2NbHMSP; Soares_NFL_T_GBC_S1; Soares_testis_NHT; Soares fetal liver spleen 1NFLS; NCI_CGAP_Mel3; Human epidermal keratinocyte; Infant brain, Bento Soares; NCI_CGAP_Kid8; NCI_CGAP_Ut4; Human Colon Cancer,re-excision; Synovial Fibroblasts (Il1/TNF), subt; Human Prostate; Gessler Wilms tumor; Human T-cell lymphoma,re-excision; Stratagene fetal spleen (#937205); L428; NCI_CGAP_Co3; Fetal Heart; NCI_CGAP_Kid11; Rejected Kidney, lib 4; Brain frontal cortex; 12 Week Early Stage Human II, Reexcision; NCI_CGAP_Kid3; Human fetal heart, Lambda ZAP Express; normalized infant brain cDNA; Hodgkin's Lymphoma II; Soares melanocyte 2NbHM; Keratinocyte; Colon Tumor II; Soares_total_fetus_Nb2HF8_9w; Soares_NhHMPu_S1 and NCI_CGAP_GCB1.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be

useful for the diagnosis, prevention, and/or treatment of neurological disorders; particularly brain cancer and neurodegenerative disorders (such as Alzheimer's, Parkinson's and Huntington's Disease). See "Neural Activity and Neurological Diseases" section, infra.

FEATURES OF PROTEIN ENCODED BY GENE NO: 70

This gene is expressed in the following tissues/cDNA libraries: normalized infant brain cDNA; Soares infant brain 1NIB and to a lesser extent in Soares fetal liver spleen 1NFLS; NCI_CGAP_Kid11; NCI_CGAP_GC6; Human Thymus Stromal Cells; NCI_CGAP_Lu24; Breast, Normal: (4005522B2); Soares breast 3NbHBst; Human Fetal Kidney, Reexcision; NCI_CGAP_Brn25; Stratagene lung (#937210); NCI_CGAP_Lu5; NCI_CGAP_Kid12; Normalized infant brain, Bento Soares; Human Skeletal Muscle; Human retina cDNA randomly primed sublibrary; Human Ovarian Cancer(#9807G017); Stromal cells(HBM3.18); Human Synovium; Human Soleus; Human adult (K.Okubo); Alzheimers, spongy change; H Female Bladder, Adult; NCI_CGAP_Ut2; Spinal Cord, re-excision; Healing groin wound - zero hr post-incision (control); Healing groin wound, 7.5 hours post incision; NCI_CGAP_Co3; Macrophage-oxLDL, re-excision; Human Testes, Reexcision; Soares retina N2b4HR; H. Frontal cortex,epileptic,re-excision; Colon Tumor II; Soares_NFL_T_GBC_S1; Soares_testis_NHT and NCI_CGAP_Sub1.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of neurological disorders; particularly brain cancer and neurodegenerative disorders (such as Alzheimer's, Parkinson's and Huntington's Disease). See "Neural Activity and Neurological Diseases" section, infra.

FEATURES OF PROTEIN ENCODED BY GENE NO: 71

This gene is expressed in the following tissues/cDNA libraries: T-Cell PHA 16 hrs; CD34 positive cells (Cord Blood).

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be

useful for the diagnosis, prevention, and/or treatment of immune system disorders; particularly immune cell proliferative disorders (e.g. leukemia), autoimmune disorders, and immunodeficiencies (including immunodeficiencies caused by genetic factors, microbial pathogens (e.g. HIV), chemotherapy, and radiation). See "Immune Activity" section, infra.

FEATURES OF PROTEIN ENCODED BY GENE NO: 72

This gene is expressed in Neutrophils control, re-excision.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of immune system disorders; particularly immune cell proliferative disorders (e.g. leukemia), autoimmune disorders, and immunodeficiencies (including immunodeficiencies caused by genetic factors, microbial pathogens (e.g. HIV), chemotherapy, and radiation). See "Immune Activity" section, infra.

FEATURES OF PROTEIN ENCODED BY GENE NO: 73

This gene is expressed in Dendritic Cells From CD34 Cells.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of immune system disorders; particularly immune cell proliferative disorders (e.g. leukemia), autoimmune disorders, and immunodeficiencies (including immunodeficiencies caused by genetic factors, microbial pathogens (e.g. HIV), chemotherapy, and radiation). See "Immune Activity" section, infra.

FEATURES OF PROTEIN ENCODED BY GENE NO: 74

This gene is expressed in Neutrophils control, re-excision.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of immune system disorders; particularly immune cell proliferative disorders (e.g. leukemia), autoimmune

disorders, and immunodeficiencies (including immunodeficiencies caused by genetic factors, microbial pathogens (e.g. HIV), chemotherapy, and radiation). See "Immune Activity" section, infra.

FEATURES OF PROTEIN ENCODED BY GENE NO: 75

The computer algorithm BLASTX has been used to determine that the translation product of this gene shares sequence homology with, as a non-limiting example, the sequence accessible through the following database accession no. sp|Q14154|Y141_HUMAN (all information available through the recited accession number is incorporated herein by reference). Preferred polypeptides of the invention comprise a polypeptide having the amino acid sequence set out in the sequence listing as SEQ ID NO:439.

This gene is expressed in the following tissues/cDNA libraries: Human Activated T-Cells; Human Adult Heart,re-excision and to a lesser extent in Stratagene colon (#937204); Primary Dendritic Cells, lib 1; Macrophage-oxLDL, re-excision; breast lymph node CDNA library; Human Thymus Stromal Cells; Bone Marrow Cell Line (RS4,11); H Umbilical Vein Endothelial Cells, frac A, re-excision; Human (Caco-2) cell line, adenocarcinoma, colon, remake; Human OB HOS control fraction I; Early Stage Human Lung, subtracted; Breast Lymph node cDNA library; Cem cells cyclohexamide treated; Human Tonsils, Lib 2; Stratagene schizo brain S11; human corpus colosum; Smooth muscle, IL1b induced; Human Stomach,re-excision; Human Adult Small Intestine; Human Infant Brain; Human Thymus; Human Umbilical Vein Endothelial Cells, uninduced; Macrophage (GM-CSF treated); Healing groin wound, 6.5 hours post incision; Smooth muscle, serum treated; NCI_CGAP_Co8; Rejected Kidney, lib 4; Adipocytes; Myoloid Progenitor Cell Line; Endothelial-induced; Endothelial cells-control; Human Microvascular Endothelial Cells, fract. A; Hodgkin's Lymphoma II; Soares melanocyte 2NbHM; Human Cerebellum; NCI_CGAP_GCB1 and Soares infant brain 1NIB.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of immune system disorders;

particularly immune cell proliferative disorders (e.g. leukemia), autoimmune disorders, and immunodeficiencies (including immunodeficiencies caused by genetic factors, microbial pathogens (e.g. HIV), chemotherapy, and radiation). See "Immune Activity" section, infra. The tissue distribution also indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of cardiovascular disorders; particularly heart disease, high blood pressure, cardiac ischemia, and coronary artery disease. See "Cardiovascular Disorders" section, infra.

FEATURES OF PROTEIN ENCODED BY GENE NO: 76

The computer algorithm BLASTX has been used to determine that the translation product of this gene shares sequence homology with, as a non-limiting example, the sequence accessible through the following database accession no. pir|S14351|C1HUQC (all information available through the recited accession number is incorporated herein by reference) which is described therein as "complement subcomponent C1q chain C precursor - human". Based on the structural similarity these homologous polypeptides are expected to share at least some biological activities. Such activities are known in the art, some of which are described elsewhere herein. Assays for determining such activities are also known in the art, some of which have been described elsewhere herein. Preferred polypeptides of the invention comprise a polypeptide having the amino acid sequence set out in the sequence listing as SEQ ID NO: 440 .

This gene is expressed in the following tissues/cDNA libraries: Primary Dendritic Cells, lib 1 and to a lesser extent in Primary Dendritic cells,frac 2; Spleen, Chronic lymphocytic leukemia; Soares fetal liver spleen 1NFLS; Colon Tumor II; NCI_CGAP_Co8; Human Placenta; Human Adult Pulmonary,re-excision; Soares placenta Nb2HP; Colon Normal II; Soares_fetal_heart_NbHH19W; Human Pancreas Tumor; Soares breast 2NbHBst; Human Adipose; NCI_CGAP_Pan1; Human Placenta (re-excision); Ovary, Cancer: (4004576 A8); Human T-Cell Lymphoma; Soares breast 3NbHBst; Human Pancreas Tumor, Reexcision; Normal colon; human tonsils; Soares infant brain 1NIB; Human Spleen; Human Chronic Synovitis; Human Thymus; CD40 activated monocyte dendridic cells; Hemangiopericytoma; Human

Fetal Brain; Stratagene liver (#937224); Colon Tumor; Rejected Kidney, lib 4; Ovary, Cancer (9809C332): Poorly differentiated adenocarcinoma; Human Fetal Kidney, Reexcision; Soares_placenta_8to9weeks_2NbHP8to9W; Colon Normal III; b4HB3MA-Cot109+10-Bio; Human Resting Macrophage; Human Thymus; Human Adult Lymph Node, subtracted; Human Fetal Brain, normalized C500H; Human Adult Skeletal Muscle; Prostate BPH,Lib 2, subtracted; Infant brain, LLNL array of Dr. M. Soares 1NIB; Tongue carcinoma; Human Gastrocnemius; Human fetal lung; STRIATUM DEPRESSION; Lung, Normal: (4005313 B1); NCI_CGAP_Eso2; Normalized infant brain, Bento Soares; stomach cancer (human); Barstead spleen HPLRB2; NCI_CGAP_Lu24; SKIN; stromal cell clone 2.5; NCI_CGAP_Lu1; Human Pituitary, subtracted; Human Lung; NCI_CGAP_Ut3; Human Synovium; NCI_CGAP_Co9; Breast, Cancer: (4005522 A2); Patient #6 Acute Myeloid Leukemia/SGAH; B Cell lymphoma; NCI_CGAP_Co14; Human Osteosarcoma; Human Colon, re-excision; Human Adipose Tissue, re-excision; wilm's tumor; Spleen metastic melanoma; Breast, Cancer: (4004943 A5); Breast, Normal: (4005522B2); Brain Frontal Cortex, re-excision; NCI_CGAP_Ut1; NCI_CGAP_Kid6; Ovary, Cancer: (4004332 A2); Clontech human aorta polyA+ mRNA (#6572); Human Fetal Dura Mater; Ulcerative Colitis; Liver Normal Met5No; Human Gall Bladder; Human Liver, normal; Fetal Liver, subtraction II; Palate normal; Fetal Heart; Bone Marrow Stromal Cell, untreated; Colon, normal; Stomach Normal; Human Placenta; Pancreas normal PCA4 No; NCI_CGAP_Brn25; NCI_CGAP_Kid5; Human Bone Marrow, treated; Soares ovary tumor NbHOT; NCI_CGAP_Lu5; Hodgkin's Lymphoma II; Soares_pregnant_uterus_NbHPU; Soares_NFL_T_GBC_S1; Soares_testis_NHT and NCI_CGAP_Ov39.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of immune system disorders; particularly immune cell proliferative disorders (e.g. leukemia), autoimmune disorders, and immunodeficiencies (including immunodeficiencies caused by genetic factors, microbial pathogens (e.g. HIV), chemotherapy, and radiation). See "Immune Activity" section, infra.

FEATURES OF PROTEIN ENCODED BY GENE NO: 77

This gene is expressed in the following tissues/cDNA libraries: Soares_fetal_liver_spleen_1NFLS_S1 and to a lesser extent in NCI_CGAP_Brn25; Soares_testis_NHT; Soares_pregnant_uterus_NbHPU; NCI_CGAP_Kid12; Soares_senescent_fibroblasts_NbHSF; NCI_CGAP_Kid3; Human Fetal Brain, normalized CO; NCI_CGAP_Lu19; NCI_CGAP_Lu24; NCI_CGAP_Thy1; H. Kidney Cortex, subtracted; Breast, Normal: (4005522B2); Colon Tumor; NCI_CGAP_Kid6; NCI_CGAP_Gas4; Human Prostate Cancer, Stage B2, re-excision; NCI_CGAP_Br2; Human Chondrosarcoma; Soares adult brain N2b5HB55Y; Olfactory epithelium,nasalcavity; NCI_CGAP_Co3; NCI_CGAP_GC6; Pancreas Islet Cell Tumor; Spleen, Chronic lymphocytic leukemia; HM3; H. Frontal cortex,epileptic,re-excision; Human Endometrial Tumor; Keratinocyte; Soares_fetal_lung_NbHL19W; Colon Normal III; Soares_NFL_T_GBC_S1; Soares_fetal_heart_NbHH19W; Soares_NhHMPu_S1 and Soares fetal liver spleen 1NFLS.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene would be useful for the diagnosis, prevention, and or treatment of liver disorders and cancers. For example, the protein can be used for the detection, treatment, and/or prevention of Wilson's disease, cirrhosis, fibrosis, bilirubin metabolism, hepatomegaly, cholestasis, liver cancer (for example, hepatoblastoma), jaundice, hepatitis (acuta and chronic) and liver metabolic diseases and conditions attributable to the differentiation of hepatocyte progenitor cells.

FEATURES OF PROTEIN ENCODED BY GENE NO: 78

The computer algorithm BLASTX has been used to determine that the translation product of this gene shares sequence homology with, as a non-limiting example, the sequence accessible through the following database accession no. sp|Q9UJM5|Q9UJM5 (all information available through the recited accession number is incorporated herein by reference) which is described therein as "DJ20N2.5 (NOVEL PROTEIN SIMILAR TO FUCOSIDASE, ALPHA-L-1, TISSUE (EC 3.2.1.51, ALPHA-L-FUCOSIDASE FUCOHYDROLASE))." Based on the structural similarity these homologous polypeptides are expected to share at least some

biological activities. Such activities are known in the art, some of which are described elsewhere herein. Assays for determining such activities are also known in the art, some of which have been described elsewhere herein. Preferred polypeptides of the invention comprise a polypeptide having the amino acid sequence set out in the sequence listing as SEQ ID NO: 441, SEQ ID NO: 442 and/or SEQ ID NO: 443 .

This gene is expressed in the following tissues/cDNA libraries: Patient#2 Acute Myeloid Leukemia/SGAH; NTERA2 + retinoic acid, 14 days; NTERA2 teratocarcinoma cell line+retinoic acid (14 days).

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of immune system disorders; particularly immune cell proliferative disorders (e.g. leukemia), autoimmune disorders, and immunodeficiencies (including immunodeficiencies caused by genetic factors, microbial pathogens (e.g. HIV), chemotherapy, and radiation). See "Immune Activity" section, infra.

FEATURES OF PROTEIN ENCODED BY GENE NO: 79

The computer algorithm BLASTX has been used to determine that the translation product of this gene shares sequence homology with, as a non-limiting example, the sequence accessible through the following Genbank database accession no. sp|O75827|O75827 (all information available through the recited accession number is incorporated herein by reference) which is described therein as "DJ71L16.5 (KIAA0267 LIKE PUTATIVE NA(+)/H(+) EXCHANGER) (FRAGMENT). Based on the structural similarity these homologous polypeptides are expected to share at least some biological activities. Such activities are known in the art, some of which are described elsewhere herein. Assays for determining such activities are also known in the art, some of which have been described elsewhere herein. Preferred polypeptides of the invention comprise a polypeptide having the amino acid sequence set out in the sequence listing as SEQ ID NO: 444 .

This gene is expressed in the following tissues/cDNA libraries: Soares_NhHMPu_S1 and to a lesser extent in Soares_pregnant_uterus_NbHPU; Soares_fetal_heart_NbHH19W; Soares_total_fetus_Nb2HF8_9w;

Soares_fetal_liver_spleen_1NFLS_S1; Soares breast 3NbHBst; NCI_CGAP_Kid11; NCI_CGAP_GC6; Soares_fetal_lung_NbHL19W; Soares placenta Nb2HP; NCI_CGAP_CNS1; Larynx Carcinoma; Human Prostate BPH, re-excision; NCI_CGAP_Kid12; NCI_CGAP_Brn35; Early Stage Human Lung, subtracted; Human Tonsils, Lib 2; Human Osteoblasts II; CD40 activated monocyte dendridic cells; Human Adipose; Human blood platelets; Human Synovial Sarcoma; NTERA2, control; Soares_multiple_sclerosis_2NbHMSP; Spleen, Chronic lymphocytic leukemia; Soares_parathyroid_tumor_NbHPA; NCI_CGAP_Sub4 and NCI_CGAP_Sub6.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of cancer and other hyperproliferative disorders (e.g., see "Hyperproliferative Disorders" section, infra). The tissue distribution also indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of reproductive system disorders; particularly male and female infertility, placental and uterine disorders (e.g. endometriosis), and cancer of reproductive organs (e.g. testicular and ovarian cancer). See "Reproductive System Disorders" section, infra.

FEATURES OF PROTEIN ENCODED BY GENE NO: 80

This gene is expressed in Monocyte activated, re-excision.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of immune system disorders; particularly immune cell proliferative disorders (e.g. leukemia), autoimmune disorders, and immunodeficiencies (including immunodeficiencies caused by genetic factors, microbial pathogens (e.g. HIV), chemotherapy, and radiation). See "Immune Activity" section, infra.

FEATURES OF PROTEIN ENCODED BY GENE NO: 81

This gene is expressed in the following tissues/cDNA libraries: Soares_fetal_heart_NbHH19W and to a lesser extent in Soares melanocyte 2NbHM; NCI_CGAP_Lu19; Soares breast 3NbHBst; NCI_CGAP_GCB1; NCI_CGAP_Lu5; H. Frontal cortex,epileptic,re-excision; Nine Week Old Early Stage Human; Soares infant brain 1NIB; Breast, Cancer: (4004943 A5); NCI_CGAP_Kid11; NCI_CGAP_Brn25; NCI_CGAP_Kid3; Soares_parathyroid_tumor_NbHPA; H. Whole Brain #2, re-excision; NCI_CGAP_Co3; Palate carcinoma; Human Fetal Kidney, Reexcision; Pancreas Islet Cell Tumor; Soares_multiple_sclerosis_2NbHMSP; Soares_placenta_8to9weeks_2NbHP8to9W; Human Cerebellum; Soares_fetal_liver_spleen_1NFLS_S1; Soares_NFL_T_GBC_S1; H. Adipose Tissue; Normalized infant brain, Bento Soares; Infant brain, Bento Soares; NCI_CGAP_Lu24; Soares retina N2b5HR; Frontal lobe,dementia,re-excision; NCI_CGAP_Ut4; Adenocarcinoma of Ovary, Human Cell Line; Hepatocellular Tumor,re-excision; Breast Cancer cell line, MDA 36; NCI_CGAP_Co10; Human Amygdala,re-excision; Human Osteoclastoma, re-excision; Soares adult brain N2b4HB55Y; HEL cell line; Ovarian Cancer; Human Infant Brain; Gessler Wilms tumor; Stratagene NT2 neuronal precursor 937230; TF-1 Cell Line GM-CSF Treated; TNFR degenerate oligo; Healing groin wound - zero hr post-incision (control); Ovary, Cancer: (15799A1F) Poorly differentiated carcinoma; NCI_CGAP_Pr28; B-Cells; Human Activated T-Cells, re-excision; Soares breast 2NbHBst; Soares adult brain N2b5HB55Y; Olfactory epithelium,nasalcavity; NCI_CGAP_Pan1; Human Gall Bladder; Bone Marrow Stromal Cell, untreated; Healing groin wound, 6.5 hours post incision; Ovarian Tumor 10-3-95; Rejected Kidney, lib 4; Early Stage Human Brain; CHME Cell Line,treated 5 hrs; Myoloid Progenitor Cell Line; Primary Dendritic cells,frac 2; Human Microvascular Endothelial Cells, fract. A; NCI_CGAP_Brn23; Human Bone Marrow, treated; Soares ovary tumor NbHOT; Bone Marrow Cell Line (RS4,11); Dendritic cells, pooled; normalized infant brain cDNA; Keratinocyte; Soares_fetal_lung_NbHL19W; Soares_total_fetus_Nb2HF8_9w; Soares placenta Nb2HP; Soares fetal liver spleen 1NFLS; NCI_CGAP_Sar4 and NCI_CGAP_Sub6.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be

useful for the diagnosis, prevention, and/or treatment of cancer and other hyperproliferative disorders (e.g., see "Hyperproliferative Disorders" section, infra).

FEATURES OF PROTEIN ENCODED BY GENE NO: 82

The computer algorithm BLASTX has been used to determine that the translation product of this gene shares sequence homology with, as a non-limiting example, the sequence accessible through the following database accession no. pir|T00351|T00351 (all information available through the recited accession number is incorporated herein by reference). Based on the structural similarity these homologous polypeptides are expected to share at least some biological activities. Such activities are known in the art, some of which are described elsewhere herein. Assays for determining such activities are also known in the art, some of which have been described elsewhere herein. Preferred polypeptides of the invention comprise a polypeptide having the amino acid sequence set out in the sequence listing as SEQ ID NO: 445.

This gene is expressed in Myoloid Progenitor Cell Line.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of immune system disorders; particularly immune cell proliferative disorders (e.g. leukemia), autoimmune disorders, and immunodeficiencies (including immunodeficiencies caused by genetic factors, microbial pathogens (e.g. HIV), chemotherapy, and radiation). See "Immune Activity" section, infra.

FEATURES OF PROTEIN ENCODED BY GENE NO: 83

This gene is expressed in the following tissues/cDNA libraries: Monocyte activated; Soares_NhHMPu_S1 and to a lesser extent in H Macrophage (GM-CSF treated), re-excision; Primary Dendritic Cells, lib 1; Soares_testis_NHT; Macrophage-oxLDL; NCI_CGAP_CLL1; Macrophage (GM-CSF treated); NCI_CGAP_GC6; NCI_CGAP_Bm25; NCI_CGAP_Kid3; Soares melanocyte 2NbHM; Soares_pregnant_uterus_NbHPU; Soares_NFL_T_GBC_S1; NCI_CGAP_Lu26; Soares adult brain N2b4HB55Y; Monocyte activated, re-excision; CD40 activated

monocyte dendridic cells; NCI_CGAP_Kid11; NCI_CGAP_GC4; Activated T-Cell (12hs)/Thiouridine labelledEco; NCI_CGAP_Brn23; Soares ovary tumor NbHOT; Activated T-cell(12h)/Thiouridine-re-excision; Soares placenta Nb2HP; Human Lung Cancer; Human Brain, striatum, re-excision; Human Astrocyte; Testis, normal; NCI_CGAP_Lu19; K562 + PMA (36 hrs),re-excision; NCI_CGAP_Co16; HL-60, RA 4h, Subtracted; NCI_CGAP_HSC2; NCI_CGAP_Lu1; Human Tonsils, Lib 2; NCI_CGAP_Ut2; H. Kidney Medulla, re-excision; Gessler Wilms tumor; H. Epididiymus, caput & corpus; Colon Tumor; NCI_CGAP_Br2; Liver, Hepatoma; Human Rhabdomyosarcoma; Hemangiopericytoma; Human Activated T-Cells, re-excision; Epithelial-TNFa and INF induced; Human Whole Six Week Old Embryo; NCI_CGAP_Pan1; Macrophage-oxLDL, re-excision; Human adult testis, large inserts; CHME Cell Line,untreated; breast lymph node CDNA library; Human Adult Testes, Large Inserts, Reexcision; Colon Carcinoma; Human Synovial Sarcoma; Primary Dendritic cells,frac 2; Pancreas Islet Cell Tumor; Soares_multiple_sclerosis_2NbHMSP; Human fetal heart, Lambda ZAP Express; HM3; Keratinocyte; Soares_total_fetus_Nb2HF8_9w; Soares_fetal_heart_NbHH19W; NCI_CGAP_Ov18; NCI_CGAP_Sub3 and NCI_CGAP_Sub6.

The tissue distribution indicates polynucleotides and polypeptides corresponding to this gene, as well as antibodies against those polypeptides, may be useful for the diagnosis, prevention, and/or treatment of immune system disorders; particularly immune cell proliferative disorders (e.g. leukemia), autoimmune disorders, and immunodeficiencies (including immunodeficiencies caused by genetic factors, microbial pathogens (e.g. HIV), chemotherapy, and radiation). See "Immune Activity" section, infra.

Table 1A

Gene No.	cDNA Clone ID	ATCC Deposit No:Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
1	HAGAN08	PTA-3101 02/23/01	Uni-ZAP XR	11	1172	306	1172	335	335	198	1	17	18	91
2	HSANL54	PTA-3103 02/23/01	pSport1	12	1649	1	1649	296	296	199	1	22	23	49
2	HSANL54	PTA-3103 02/23/01	pSport1	94	1116	1	1116	286	286	281	1	22	23	49
2	HSANL54	PTA-3103 02/23/01	pSport1	95	724	198	724		2	282	1	1	2	187
3	HSYHY70	PTA-3103 02/23/01	pCMVSport 3.0	13	1965	1	1965	59	59	200	1	17	18	95
3	HSYHY70	PTA-3103 02/23/01	pCMVSport 3.0	96	636	1	636	46	46	283	1	17	18	95
4	HEOUO75	PTA-3101 02/23/01	pSport1	14	3371	1	3371	40	40	201	1	20	21	175
4	HEOUO75	PTA-3101 02/23/01	pSport1	97	1204	44	1204	72	72	284	1	20	21	175
5	HSCPC08	PTA-3103 02/23/01	pSport1	15	1214	1	1214	200	200	202	1	40	41	126
5	HSCPC08	PTA-3103 02/23/01	pSport1	98	1117	1	1117	180	180	285	1	40	41	126

Gene No.	cDNA Clone ID	ATCC Deposit No:Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
6	HSCPT22	PTA-3103 02/23/01	pSport1	16	896	1	896	92	92	203	1	26	27	187
6	HSCPT22	PTA-3103 02/23/01	pSport1	99	1092	1	1092	81	81	286	1	26	27	187
7	HTLED86	PTA-3103 02/23/01	Uni-ZAP XR	17	1299	1	1299	545	545	204	1	15	16	38
7	HTLED86	PTA-3103 02/23/01	Uni-ZAP XR	100	1450	678	1450	809	809	287	1	26	27	214
7	HTLED86	PTA-3103 02/23/01	Uni-ZAP XR	101	764	1	764		1	288	1	8	9	254
8	HTPKP89	PTA-3103 02/23/01	Uni-ZAP XR	18	1796	1	1796	70	70	205	1	28	29	163
8	HTPKP89	PTA-3103 02/23/01	Uni-ZAP XR	102	880	1	880	61	61	289	1	28	29	221
9	HSRFP52	PTA-3103 02/23/01	Uni-ZAP XR	19	1881	13	1318	174	174	206	1	21	22	369
9	HSRFP52	PTA-3103 02/23/01	Uni-ZAP XR	103	1321	1	1321	169	169	290	1	21	22	135
9	HSRFP52	PTA-3103 02/23/01	Uni-ZAP XR	104	1558	361	994	72	72	291	1	1	2	295
10	HDHEA83	PTA-3101 02/23/01	pCMVSport 2.0	20	2618	1	2618	42	42	207	1	24	25	85

Gene No.	cDNA Clone ID	ATCC Deposit No:Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
10	HDHEA83	PTA-3101 02/23/01	pCMVSport 2.0	105	2079	1	2079	91	91	292	1	24	25	85
10	HDHEA83	PTA-3101 02/23/01	pCMVSport 2.0	106	3144	822	1185		166	293	1	1	2	196
10	HDHEA83	PTA-3101 02/23/01	pCMVSport 2.0	107	843	1	843		649	294	1	11	12	58
11	HFXBR92	PTA-3101 02/23/01	Lambda ZAP II	21	1549	1	1549	225	225	208	1	23	24	172
11	HFXBR92	PTA-3101 02/23/01	Lambda ZAP II	108	613	1	613	213	213	295	1	23	24	133
11	HFXBR92	PTA-3101 02/23/01	Lambda ZAP II	109	945	374	945		341	296	1	1	2	74
12	HSYIH77	PTA-3103 02/23/01	pCMVSport 3.0	22	3239	1	3239	62	62	209	1	45	46	829
12	HSYIH77	PTA-3103 02/23/01	pCMVSport 3.0	110	450	1	450	50	50	297	1	45	46	133
13	HTAHS92	PTA-3103 02/23/01	Uni-ZAP XR	23	1433	1	1433	65	65	210	1	21	22	108
13	HTAHS92	PTA-3103 02/23/01	Uni-ZAP XR	111	773	136	773	193	193	298	1	21	22	108
13	HTAHS92	PTA-3103 02/23/01	Uni-ZAP XR	112	830	1	830		25	299	1	1	2	68

Gene No.	cDNA Clone ID	ATCC Deposit No:Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
14	HAROV59	PTA-3101 02/23/01	pCMVSport 3.0	24	2517	1	2517	49	49	211	1	18	19	153
14	HAROV59	PTA-3101 02/23/01	pCMVSport 3.0	113	646	1	646	39	39	300	1	18	19	194
15	HDCCG73	PTA-3101 02/23/01	pSport1	25	807	1	807	45	45	212	1	14	15	87
15	HDCCG73	PTA-3101 02/23/01	pSport1	114	739	1	739	100	100	301	1	14	15	87
16	HQAHD50	PTA-3103 02/23/01	pCMVSport 3.0	26	554	1	554	184	184	213	1	39	40	90
16	HQAHD50	PTA-3103 02/23/01	pCMVSport 3.0	115	529	1	529	157	157	302	1	39	40	90
17	HROBA16	PTA-3103 02/23/01	Uni-ZAP XR	27	1319	1	1319	317	317	214	1	31	32	34
17	HROBA16	PTA-3103 02/23/01	Uni-ZAP XR	116	751	1	751	342	342	303	1	31	32	34
17	HROBA16	PTA-3103 02/23/01	Uni-ZAP XR	117	660	1	660		322	304	1	1	2	47
18	HTPJD12	PTA-3103 02/23/01	Uni-ZAP XR	28	1487	1	1487	23	23	215	1	17	18	245
18	HTPJD12	PTA-3103 02/23/01	Uni-ZAP XR	118	1488	6	1488	21	21	305	1	17	18	245

Gene No.	cDNA Clone ID	ATCC Deposit No:Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
19	HHAWD13	PTA-3101 02/23/01	pCMVSport 3.0	29	1889	1	1889	261	261	216	1	15	16	459
19	HHAWD13	PTA-3101 02/23/01	pCMVSport 3.0	119	656	1	656	235	235	306	1	15	16	140
20	HISFI83	PTA-3102 02/23/01	pSport1	30	1192	1	1192	145	145	217	1	33	34	110
20	HISFI83	PTA-3102 02/23/01	pSport1	120	1394	155	1394	287	287	307	1	33	34	110
21	HISFV70	PTA-3102 02/23/01	pSport1	31	1162	1	1162	71	71	218	1	20	21	107
21	HISFV70	PTA-3102 02/23/01	pSport1	121	1164	43	1164	99	99	308	1	20	21	107
22	HNSAB41	PTA-3102 02/23/01	pSport1	32	2799	1	2799	221	221	219	1	35	36	428
22	HNSAB41	PTA-3102 02/23/01	pSport1	122	2793	1	2793	206	206	309	1	35	36	251
23	HOCNY94	PTA-3103 02/23/01	pSport1	33	1656	1	1656	100	100	220	1	25	26	124
23	HOCNY94	PTA-3103 02/23/01	pSport1	123	511	1	511	86	86	310	1	25	26	124
24	HAROG72	PTA-3101 02/23/01	pCMVSport 3.0	34	2051	1	2051	230	230	221	1	31	32	87

Gene No.	cDNA Clone ID	ATCC Deposit No:Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
24	HAROG72	PTA-3101 02/23/01	pCMVSport 3.0	124	581	1	581	215	215	311	1	31	32	87
25	HDACT07	PTA-3101 02/23/01	pSport1	35	2053	1	2053	28	28	222	1	26	27	84
25	HDACT07	PTA-3101 02/23/01	pSport1	125	1166	496	1166	513	513	312	1	26	27	84
26	HLTIJ80	PTA-3102 02/23/01	Uni-ZAP XR	36	576	1	576	111	111	223	1	22	23	76
26	HLTIJ80	PTA-3102 02/23/01	Uni-ZAP XR	126	692	1	692		3	313	1	1	2	71
27	HNTZG72	PTA-3103 02/23/01	pSport1	37	1290	1	1290	95	95	224	1	19	20	142
27	HNTZG72	PTA-3103 02/23/01	pSport1	127	675	1	675	76	76	314	1	19	20	142
28	HNUCE33	PTA-3103 02/23/01	pCMVSport 3.0	38	1322	1	1322	341	341	225	1	30	31	84
28	HNUCE33	PTA-3103 02/23/01	pCMVSport 3.0	128	3669	2413	3669	2743	2743	315	1	30	31	84
29	HODEM32	PTA-3103 02/23/01	Uni-ZAP XR	39	1877	1	1877	399	399	226	1	22	23	88
29	HODEM32	PTA-3103 02/23/01	Uni-ZAP XR	129	667	1	667	387	387	316	1	22	23	88

Gene No.	cDNA Clone ID	ATCC Deposit No:Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
30	HPJHQ20	PTA-3103 02/23/01	Uni-ZAP XR	40	2559	1	2559	70	70	227	1	24	25	127
30	HPJHQ20	PTA-3103 02/23/01	Uni-ZAP XR	130	561	1	561	57	57	317	1	24	25	127
31	HQADO95	PTA-3103 02/23/01	pCMVSport 3.0	41	2116	1	2116	122	122	228	1	23	24	83
31	HQADO95	PTA-3103 02/23/01	pCMVSport 3.0	131	702	1	702	107	107	318	1	23	24	83
32	HTENS88	PTA-3103 02/23/01	Uni-ZAP XR	42	1352	1	1352	233	233	229	1	21	22	114
32	HTENS88	PTA-3103 02/23/01	Uni-ZAP XR	132	483	1	483	226	226	319	1	21	22	86
32	HTENS88	PTA-3103 02/23/01	Uni-ZAP XR	133	748	1	748		1	320	1	1	2	70
33	HTLGC03	PTA-3103 02/23/01	Uni-ZAP XR	43	1532	1	1532	264	264	230	1	20	21	81
33	HTLGC03	PTA-3103 02/23/01	Uni-ZAP XR	134	652	1	652	257	257	321	1	20	21	81
33	HTLGC03	PTA-3103 02/23/01	Uni-ZAP XR	135	3006	16	824		2109	322	1			2
34	HTLKQ55	PTA-3103 02/23/01	Uni-ZAP XR	44	1300	1	1300	261	261	231	1	29	30	273

Gene No.	cDNA Clone ID	ATCC Deposit No:Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
34	HTLKQ55	PTA-3103 02/23/01	Uni-ZAP XR	136	720	1	720	249	249	323	1	29	30	138
35	HTOJF42	PTA-3103 02/23/01	Uni-ZAP XR	45	2564	1	2564	96	96	232	1	21	22	112
35	HTOJF42	PTA-3103 02/23/01	Uni-ZAP XR	137	463	1	463	91	91	324	1	21	22	124
36	HTPHC19	PTA-3103 02/23/01	Uni-ZAP XR	46	2594	1	2594	225	225	233	1	25	26	82
36	HTPHC19	PTA-3103 02/23/01	Uni-ZAP XR	138	699	186	699	397	397	325	1	25	26	82
37	HDPHG50	PTA-3101 02/23/01	pCMVSport 3.0	47	2030	1	2030	200	200	234	1	42	43	136
37	HDPHG50	PTA-3101 02/23/01	pCMVSport 3.0	139	950	1	950	205	205	326	1	37	38	248
37	HDPHG50	PTA-3101 02/23/01	pCMVSport 3.0	140	2952	735	2952		2773	327	1	19	20	27
38	HHEWS13	PTA-3102 02/23/01	pCMVSport 3.0	48	1602	1	1602	420	420	235	1	38	39	47
38	HHEWS13	PTA-3102 02/23/01	pCMVSport 3.0	141	776	1	776	410	410	328	1	36	37	51
39	HOGCY01	PTA-3103 02/23/01	pCMVSport 2.0	49	508	1	508	141	141	236	1	37	38	122

Gene No.	cDNA Clone ID	ATCC Deposit No:Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
40	HPJGT38	PTA-3103 02/23/01	Uni-ZAP XR	50	612	1	612	6	6	237	1	43	44	90
41	HTFMK11	PTA-3103 02/23/01	pSport1	51	2291	1	2291	429	429	238	1	25	26	33
41	HTFMK11	PTA-3103 02/23/01	pSport1	142	702	1	702	476	476	329	1	25	26	33
41	HTFMK11	PTA-3103 02/23/01	pSport1	143	798	1	798		3	330	1	1	2	99
42	HTSGQ95	PTA-3103 02/23/01	pBluescript	52	2842	1	2842	88	88	239	1	23	24	35
42	HTSGQ95	PTA-3103 02/23/01	pBluescript	144	566	1	566	88	88	331	1	24	25	35
42	HTSGQ95	PTA-3103 02/23/01	pBluescript	145	1939	366	466		1153	332	1	1	2	262
43	HLSAI43	PTA-3102 02/23/01	pSport1	53	765	1	765	191	191	240	1	25	26	82
43	HLSAI43	PTA-3102 02/23/01	pSport1	146	619	1	619	181	181	333	1	25	26	82
44	HNBTF02	PTA-3102 02/23/01	pSport1	54	1896	1	1896	32	32	241	1	22	23	219
44	HNBTF02	PTA-3102 02/23/01	pSport1	147	2032	140	2032	154	154	334	1	22	23	587

Gene No.	cDNA Clone ID	ATCC Deposit No:Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
45	HNSCC06	PTA-3102 02/23/01	pSport1	55	1876	1	1876	25	25	242	1	15	16	181
45	HNSCC06	PTA-3102 02/23/01	pSport1	148	1048	1	1048	8	8	335	1	15	16	337
46	HTENQ40	PTA-3103 02/23/01	Uni-ZAP XR	56	1072	1	1072	84	84	243	1	44	45	125
46	HTENQ40	PTA-3103 02/23/01	Uni-ZAP XR	149	701	1	701	77	77	336	1	44	45	125
47	HCNCM78	PTA-3101 02/23/01	Lambda ZAP II	57	652	1	652	34	34	244	1	24	25	132
47	HCNCM78	PTA-3101 02/23/01	Lambda ZAP II	150	617	1	617	24	24	337	1	24	25	132
47	HCNCM78	PTA-3101 02/23/01	Lambda ZAP II	151	881	76	881	55	55	338	1	24	25	81
48	HCOKD57	PTA-3101 02/23/01	pSport1	58	1352	1	1352	64	64	245	1	24	25	186
48	HCOKD57	PTA-3101 02/23/01	pSport1	152	576	1	576	54	54	339	1	24	25	173
49	HRAEO74	PTA-3103 02/23/01	pCMVSport 3.0	59	1335	393	1335	545	545	246	1	22	23	114
50	HTACM88	PTA-3103 02/23/01	Uni-ZAP XR	60	2140	1	2140	64	64	247	1	25	26	91

Gene No.	cDNA Clone ID	ATCC Deposit No:Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
50	HTACM88	PTA-3103 02/23/01	Uni-ZAP XR	153	637	1	637	64	64	340	1	25	26	91
50	HTACM88	PTA-3103 02/23/01	Uni-ZAP XR	154	800	1	777		332	341	1	1	2	139
51	HBWBI44	PTA-3101 02/23/01	ZAP Express	61	257	1	257	39	39	248	1	17	18	73
51	HBWBI44	PTA-3101 02/23/01	ZAP Express	155	684	1	684	425	425	342	1	17	18	86
52	HAGIF61	PTA-3101 02/23/01	Uni-ZAP XR	62	684	1	684	160	160	249	1	28	29	118
52	HAGIF61	PTA-3101 02/23/01	Uni-ZAP XR	156	1574	863	1574	1015	1015	343	1	28	29	118
53	HSYHD12	PTA-3103 02/23/01	pCMVSport 3.0	63	1977	1	1977	301	301	250	1	19	20	466
53	HSYHD12	PTA-3103 02/23/01	pCMVSport 3.0	157	2050	30	2050	312	312	344	1	19	20	365
54	HTAGF12	PTA-3103 02/23/01	Uni-ZAP XR	64	2632	1	2632	305	305	251	1	17	18	62
54	HTAGF12	PTA-3103 02/23/01	Uni-ZAP XR	158	638	1	638	298	298	345	1	17	18	62
54	HTAGF12	PTA-3103 02/23/01	Uni-ZAP XR	159	1332	81	792		28	346	1	13	14	18

Gene No.	cDNA Clone ID	ATCC Deposit No:Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
55	HTHCA16	PTA-3103 02/23/01	Uni-ZAP XR	65	1241	1	1241	77	77	252	1	20	21	306
55	HTHCA16	PTA-3103 02/23/01	Uni-ZAP XR	160	1267	41	1267	99	99	347	1	20	21	306
56	HNFIQ15	PTA-3102 02/23/01	pBluescrip t	66	1154	1	1111	105	105	253	1	26	27	191
56	HNFIQ15	PTA-3102 02/23/01	pBluescrip t	161	476	1	476	105	105	348	1	26	27	106
56	HNFIQ15	PTA-3102 02/23/01	pBluescrip t	162	1040	664	986		417	349	1	1	2	137
56	HNFIQ15	PTA-3102 02/23/01	pBluescrip t	163	621	1	621		255	350	1	1	2	102
57	HNHPS28	PTA-3102 02/23/01	Uni-ZAP XR	67	1077	1	1077	208	208	254	1	15	16	146
57	HNHPS28	PTA-3102 02/23/01	Uni-ZAP XR	164	601	1	601	201	201	351	1	15	16	133
58	HNTDN59	PTA-3102 02/23/01	pCMVSpo rt 3.0	68	3067	1	3067	117	117	255	1	15	16	777
58	HNTDN59	PTA-3102 02/23/01	pCMVSpo rt 3.0	165	3337	1	3337	106	106	352	1	15	16	136
58	HNTDN59	PTA-3102 02/23/01	pCMVSpo rt 3.0	166	510	1	510	107	107	353	1	15	16	134

Gene No.	cDNA Clone ID	ATCC Deposit No:Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
58	HNTDN59	PTA-3102 02/23/01	pCMVSport 3.0	167	1367	682	1323		1	354	1	1	2	303
59	HNTQM17	PTA-3102 02/23/01	pSport1	69	3453	1	3453	251	251	256	1	31	32	217
59	HNTQM17	PTA-3102 02/23/01	pSport1	168	594	1	594	241	241	355	1	31	32	118
60	HNTTF76	PTA-3102 02/23/01	pSport1	70	1109	1	1109	59	59	257	1	24	25	93
60	HNTTF76	PTA-3102 02/23/01	pSport1	169	684	1	684	48	48	356	1	24	25	93
61	HCFGD60	PTA-3101 02/23/01	pSport1	71	1158	1	1158	137	137	258	1	48	49	122
61	HCFGD60	PTA-3101 02/23/01	pSport1	170	1494	378	1494	496	496	357	1	48	49	122
62	HMUEP30	PTA-3102 02/23/01	pCMVSport 3.0	72	1269	1	1269	251	251	259	1	42	43	113
62	HMUEP30	PTA-3102 02/23/01	pCMVSport 3.0	171	610	1	610	241	241	358	1	42	43	95
63	HNSCA10	PTA-3102 02/23/01	pSport1	73	2911	1	2911	279	279	260	1	33	34	215
63	HNSCA10	PTA-3102 02/23/01	pSport1	172	654	1	654	266	266	359	1	33	34	129

Gene No.	cDNA Clone ID	ATCC Deposit No:Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
64	HTPAO67	PTA-3103 02/23/01	Uni-ZAP XR	74	5023	2522	5017	2709	2709	261	1	27	28	84
64	HTPAO67	PTA-3103 02/23/01	Uni-ZAP XR	173	2046	1392	2046	1579	1579	360	1	33	34	84
64	HTPAO67	PTA-3103 02/23/01	Uni-ZAP XR	174	1439	446	1433		6	361	1	1	2	88
65	HAZCB15	PTA-3101 02/23/01	pCMVSport 3.0	75	1129	1	1129	32	32	262	1	22	23	116
65	HAZCB15	PTA-3101 02/23/01	pCMVSport 3.0	175	675	1	675	7	7	362	1	22	23	116
66	HSLFK66	PTA-3103 02/23/01	Uni-ZAP XR	76	1889	1	1889	167	167	263	1	39	40	139
66	HSLFK66	PTA-3103 02/23/01	Uni-ZAP XR	176	8446	2451	8446	2610	2610	363	1	39	40	139
67	HCFPE46	PTA-3101 02/23/01	pSport1	77	845	1	845	151	151	264	1	18	19	82
67	HCFPE46	PTA-3101 02/23/01	pSport1	177	730	1	730	140	140	364	1	18	19	82
68	HNGPB91	PTA-3102 02/23/01	Uni-ZAP XR	78	1799	1	1799	83	83	265	1	22	23	59
68	HNGPB91	PTA-3102 02/23/01	Uni-ZAP XR	178	621	1	621	70	70	365	1	22	23	59

Gene No.	cDNA Clone ID	ATCC Deposit No:Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
68	HNGPB91	PTA-3102 02/23/01	Uni-ZAP XR	179	558	1	558	111	111	366	1	1	2	101
69	HRADV31	PTA-3103 02/23/01	pCMVSport 3.0	79	2463	1	2463	203	203	266	1	22	23	31
69	HRADV31	PTA-3103 02/23/01	pCMVSport 3.0	180	1513	1	1513	188	188	367	1	22	23	31
69	HRADV31	PTA-3103 02/23/01	pCMVSport 3.0	181	777	131	777		54	368	1	1	2	118
70	HNBVG70	PTA-3102 02/23/01	pSport1	80	1168	1	1168	273	273	267	1	48	49	87
70	HNBVG70	PTA-3102 02/23/01	pSport1	182	1909	721	1909	981	981	369	1	48	49	87
71	HCFGK19	PTA-3101 02/23/01	pSport1	81	1707	1	1707	334	334	268	1	25	26	73
71	HCFGK19	PTA-3101 02/23/01	pSport1	183	773	155	773	472	472	370	1	25	26	73
72	HNGOG04	PTA-3102 02/23/01	Uni-ZAP XR	82	1480	1	1480	27	27	269	1	21	22	81
72	HNGOG04	PTA-3102 02/23/01	Uni-ZAP XR	184	614	1	614	20	20	371	1	21	22	81
73	HDCGC29	PTA-3101 02/23/01	pSport1	83	425	1	425	269	269	270	1	31	32	52

Gene No.	cDNA Clone ID	ATCC Deposit No:Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
73	HDCGC29	PTA-3101 02/23/01	pSport1	185	437	1	437	253	253	372	1	31	32	61
74	HNGNT27	PTA-3102 02/23/01	Uni-ZAP XR	84	1732	1	1732	61	61	271	1	24	25	83
74	HNGNT27	PTA-3102 02/23/01	Uni-ZAP XR	186	587	1	587	54	54	373	1	24	25	83
75	HMUHD72	PTA-3102 02/23/01	pCMVSport 3.0	85	2131	1	2131	168	168	272	1	26	27	84
75	HMUHD72	PTA-3102 02/23/01	pCMVSport 3.0	187	1706	48	1706	204	204	374	1	26	27	84
76	HLYCK47	PTA-3102 02/23/01	pSport1	86	1143	1	1143	72	72	273	1	28	29	230
76	HLYCK47	PTA-3102 02/23/01	pSport1	188	1150	56	1150	119	119	375	1	28	29	143
76	HLYCK47	PTA-3102 02/23/01	pSport1	189	1233	45	1233	108	108	376	1	28	29	245
77	HLYFJ90	PTA-3102 02/23/01	pSport1	87	641	1	641	230	230	274	1	23	24	83
77	HLYFJ90	PTA-3102 02/23/01	pSport1	190	633	1	633	258	258	377	1	23	24	83
78	HMLHD54	PTA-3102 02/23/01	pCMVSport 3.0	88	1524	1	1524	75	75	275	1	28	29	91

Gene No.	cDNA Clone ID	ATCC Deposit No:Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
78	HMLHD54	PTA-3102 02/23/01	pCMVSport 3.0	191	705	42	705	102	102	378	1	28	29	91
79	HBPOM70	PTA-3101 02/23/01	Other	89	1810	1	1810	374	374	276	1	37	38	336
79	HBPOM70	PTA-3101 02/23/01	Other	192	2901	1	2901	373	373	379	1	37	38	336
80	HMSMO35	PTA-3102 02/23/01	Uni-ZAP XR	90	1617	1	1617	407	407	277	1	20	21	106
80	HMSMO35	PTA-3102 02/23/01	Uni-ZAP XR	193	611	1	611	395	395	380	1	21	22	72
81	HMUCI88	PTA-3102 02/23/01	pCMVSport 3.0	91	758	1	758	239	239	278	1	20	21	131
81	HMUCI88	PTA-3102 02/23/01	pCMVSport 3.0	194	3111	1593	3111	1815	1815	381	1	20	21	75
82	HMUDN51	PTA-3102 02/23/01	pCMVSport 3.0	92	2152	1	2152	54	54	279	1	40	41	81
82	HMUDN51	PTA-3102 02/23/01	pCMVSport 3.0	195	490	1	490	45	45	382	1	40	41	81
83	HMAGC36	PTA-3102 02/23/01	Uni-ZAP XR	93	758	1	758	72	72	280	1	18	19	108
83	HMAGC36	PTA-3102 02/23/01	Uni-ZAP XR	196	1527	834	1527	898	898	383	1	18	19	117

Gene No.	cDNA Clone ID	ATCC Deposit No:Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
83	HMAGC36	PTA-3102 02/23/01	Uni-ZAP XR	197	3746	1461	3746		2544	384	1	10	11	167

Table 1B

Gene No:	Clone ID NO:	Contig ID:	SEQ ID NO: X	ORF (From-To)	AA SEQ ID NO: Y	Predicted Epitopes	Tissue Distribution Library code: count (see Table IV for Library Codes)	Cytologic Band	OMIM Disease Reference(s):
1	HAGAN08	1212501	11	335 - 610	198	Pro-56 to Leu-62, Pro-86 to Asp-91.	S0010: 2, H0560: 1 and H0445: 1.		
2	HSANL54	1262040	12	296 - 445	199		S0358: 6, L0803: 6, L0794: 5, L0805: 5, L0748: 5, L0740: 5, H0144: 4, L0438: 4, L0741: 4, L0749: 4, H0556: 3, H0050: 3, H0617: 3, H0087: 3, L0769: 3, L0809: 3, L0439: 3, L0745: 3, L0747: 3, H0265: 2, H0583: 2, H0393: 2, H0013: 2, H0635: 2, H0545: 2, L0804: 2, L0789: 2, H0435: 2, H0521: 2, L0743: 2, L0756: 2, S0342: 1, H0254: 1, H0459: 1, S0420: 1, S0442: 1, S0354: 1, S0360: 1,		

							S0045: 1, S0046: 1, H0645: 1, S0222: 1, H0610: 1, H0599: 1, H0706: 1, H0036: 1, S0474: 1, H0581: 1, H0327: 1, H0051: 1, H0083: 1, H0271: 1, H0135: 1, H0090: 1, H0616: 1, H0551: 1, L0351: 1, H0494: 1, H0026: 1, L0800: 1, L0643: 1, L0764: 1, L0662: 1, L0774: 1, L0651: 1, L0806: 1, L0655: 1, L0807: 1, L0659: 1, L5622: 1, L0663: 1, H0658: 1, H0539: 1, H0710: 1, H0555: 1, S3014: 1, S0027: 1, L0744: 1, S0436: 1, L0597: 1, L0485: 1, L0366: 1, S0026: 1, H0665: 1, H0542: 1, H0543: 1 and H0422: 1.		
l		1213405	94	286 - 435	281				
		1191032	95	2 - 562	282				
3	HSYHY70	1268180	13	59 - 346	200	Gln-48 to Cys-53, Cys-64 to Gly-70,	H0556: 23, H0521: 12, H0551: 10, H0265: 8,		

						Leu-78 to Ser-83.	H0692: 8, H0543: 8, S0418: 7, L0748: 7, H0542: 7, H0318: 6, H0560: 6, S3014: 6, H0445: 6, S0436: 6, L0665: 5, L0747: 5, H0423: 5, H0341: 4, H0617: 4, S0440: 4, L0769: 4, L0439: 4, L0740: 4, L0750: 4, L0595: 4, S0278: 3, H0052: 3, H0622: 3, H0135: 3, H0040: 3, S0144: 3, L5566: 3, L0768: 3, L0766: 3, L0775: 3, L0776: 3, H0547: 3, S0328: 3, S0206: 3, L0591: 3, L0608: 3, H0422: 3, H0170: 2, H0657: 2, H0484: 2, S0408: 2, S0045: 2, S0046: 2, H0599: 2, H0545: 2, H0050: 2, H0012: 2, H0620: 2, H0083: 2, H0284: 2, H0087: 2, H0488: 2, S0150: 2, L0640: 2, L0771: 2, L0773: 2, L0521: 2,		

							L0363: 2, L0783: 2, L0383: 2, L0663: 2, L0438: 2, H0520: 2, L0751: 2, L0731: 2, L0757: 2, S0434: 2, L0596: 2, L0362: 2, T0002: 1, H0686: 1, S0040: 1, S0218: 1, H0583: 1, H0656: 1, S0180: 1, S0212: 1, H0483: 1, H0177: 1, H0125: 1, S0420: 1, S0356: 1, S0376: 1, S0444: 1, S0360: 1, H0208: 1, S0132: 1, S0476: 1, H0619: 1, H0393: 1, L0717: 1, H0586: 1, H0587: 1, H0642: 1, H0331: 1, H0256: 1, T0109: 1, H0013: 1, T0082: 1, S0182: 1, H0309: 1, T0110: 1, H0327: 1, H0544: 1, H0041: 1, S0051: 1, H0266: 1, H0290: 1, H0252: 1, H0328: 1, H0604: 1, H0031: 1, H0644: 1, H0628: 1, H0181: 1,		

							H0606: 1, S0364: 1, H0068: 1, H0090: 1, H0616: 1, H0264: 1, H0412: 1, H0059: 1, S0038: 1, H0100: 1, L0351: 1, T0042: 1, H0494: 1, H0561: 1, L0065: 1, S0438: 1, H0509: 1, S0472: 1, H0647: 1, S0422: 1, S0002: 1, S0426: 1, L0500: 1, L0637: 1, L0772: 1, L0372: 1, L0645: 1, L0662: 1, L0364: 1, L0388: 1, L0774: 1, L0375: 1, L0805: 1, L0653: 1, L0655: 1, L0657: 1, L0559: 1, L0659: 1, L0526: 1, L0382: 1, L0809: 1, L0792: 1, L0666: 1, L0664: 1, H0144: 1, H0698: 1, H0699: 1, H0703: 1, H0435: 1, S0380: 1, H0522: 1, H0696: 1, S0028: 1, L0744: 1, L0754: 1, L0779: 1, L0758: 1, L0759: 1,		

							L0593: 1, L0601: 1, S0011: 1, H0668: 1, S0276: 1 and S0424: 1.		
		1225974	96	46 - 333	283	Gln-48 to Cys-53, Cys-64 to Gly-70.			
4	HEOUO75	1283143	14	40 - 567	201	Ser-19 to Met-38, Lys-53 to Asp-60, Leu-99 to Glu-105, Glu-112 to Pro-117, Lys-122 to Arg-130, Arg-166 to Ser-171.	H0271: 15, L0667: 4, H0179: 3, S0428: 3, H0457: 2, H0416: 2, S0052: 2, S0045: 1, H0619: 1, H0041: 1, H0050: 1, H0039: 1, T0023: 1, L0372: 1, L0805: 1, S0053: 1 and S0216: 1.		
		1228107	97	72 - 599	284				
5	HSCPC08	1262036	15	200 - 580	202	Pro-121 to Asp-126.	L0749: 3, S0222: 2, H0333: 1, H0181: 1, L0769: 1, L0761: 1, L0663: 1, L0665: 1, L0750: 1, L0779: 1, H0668: 1 and H0423: 1.		
		1213061	98	180 - 560	285				
6	HSCPT22	1243895	16	92 - 655	203	Thr-74 to Asn-79, Lys-115 to Asp-120.	L0745: 2, H0616: 1, L0758: 1 and H0668: 1.		
		1209266	99	81 - 644	286	Thr-74 to Asn-79, Lys-115 to Asp-120.			
7	HTLED86	1253125	17	545 - 661	204	Cys-32 to Thr-38.	H0253: 6, L0758: 3, H0038: 2, L0774: 2,		

							L0743: 2, L0749: 2, S0040: 1, H0661: 1, S0360: 1, S0007: 1, S6026: 1, H0351: 1, H0441: 1, H0485: 1, H0618: 1, H0087: 1, H0647: 1, L0800: 1, L0794: 1, L0766: 1, S0126: 1, H0658: 1, L0748: 1, L0745: 1, L0755: 1, L0759: 1 and L0697: 1.		
		1222077	100	809 - 1450	287	His-31 to Gln-36, Ser-115 to Trp-124, Arg-168 to Ser-174.			
		1221659	101	1 - 762	288	His-13 to Gln-18, Ser-97 to Trp-106.			
8	HTPKP89	1263310	18	70 - 561	205	Pro-108 to Lys-113, Ile-157 to Arg-163.	L0777: 7, L0748: 5, L0750: 4, L0779: 3, L0805: 2, L0517: 2, L0439: 2, L0740: 2, L0747: 2, H0580: 1, S0010: 1, T0003: 1, H0622: 1, L0764: 1, H0144: 1, S3014: 1, L0749: 1 and L0758: 1.		
		1213121	102	61 - 726	289	Pro-108 to Lys-113, Ser-170 to Thr-176, Ala-190 to Ile-199.			

9	HSRFP52	1254537	19	174 - 1283	206	Asp-55 to Gln-62, Thr-103 to Arg-108, Asp-160 to Ser-170, Arg-180 to Asn-186, Ala-193 to Ala-204, Ala-222 to Pro-229, Gln-297 to Leu-304.	AR055: 10, AR060: 5, AR053: 5, AR052: 5, AR033: 5, AR061: 4, AR089: 4, AR096: 4, AR104: 2 S0022: 7, L0805: 3, H0556: 2, H0046: 2, L0764: 2, L0662: 2, L0748: 2, H0305: 1, H0013: 1, H0050: 1, H0039: 1, H0040: 1, H0087: 1, T0042: 1, L0643: 1, L0794: 1, L0803: 1, L0804: 1, L0807: 1, L0809: 1, L0666: 1, H0144: 1, L0749: 1, L0779: 1 and L0758: 1.		
		745408	103	169 - 576	290	Asp-55 to Gln-62, Pro-112 to Pro-118.			
		1182209	104	72 - 956	291	Pro-17 to Gln-24, Asp-86 to Ser-96, Arg-106 to Asn-112, Ala-119 to Ala-130, Ala-148 to Pro-155, Gln-223 to Leu-230.			
10	HDHEA83	1243831	20	42 - 299	207	Pro-65 to Ser-73.	L0439: 18, L0748: 15, L0758: 10, L0777: 9, L0803: 8, S0007: 7,		

							H0046: 7, L0750: 7, S0356: 6, S0222: 5, L0742: 5, L0747: 5, L0731: 5, H0013: 4, S0010: 4, L0769: 4, L0794: 4, L0438: 3, H0539: 3, L0756: 3, L0757: 3, S0420: 2, S0360: 2, S6028: 2, L0770: 2, L0768: 2, L0775: 2, L0659: 2, L0789: 2, H0651: 2, L0754: 2, L0759: 2, L0599: 2, H0293: 2, S0116: 1, H0351: 1, H0438: 1, H0244: 1, H0599: 1, H0253: 1, H0581: 1, H0052: 1, H0546: 1, H0545: 1, H0178: 1, H0567: 1, H0570: 1, L0471: 1, H0051: 1, S0051: 1, T0010: 1, H0687: 1, H0622: 1, H0644: 1, H0124: 1, H0591: 1, H0634: 1, L0564: 1, L0762: 1, L0761: 1, L0646: 1, L0643: 1, L0771: 1, L0773: 1,		

							L0662: 1, L0363: 1, L0649: 1, L0806: 1, L0807: 1, L0515: 1, L0783: 1, L0809: 1, L0792: 1, S0053: 1, H0144: 1, H0414: 1, H0660: 1, L0740: 1, L0745: 1, L0749: 1, L0780: 1, S0434: 1, S0436: 1, L0597: 1, L0588: 1, L0604: 1, L0601: 1, H0543: 1, H0423: 1 and H0422: 1.		
		1213580	105	91 - 348	292	Pro-65 to Ser-73.			
		1217946	106	166 - 753	293	Thr-1 to Glu-13, Arg-135 to Asp-142, Pro-186 to Thr-193.			
		1209512	107	649 - 825	294				
11	HFXBR92	1243870	21	225 - 743	208	Ser-50 to His-56, Glu-150 to Thr-160.	L0471: 3, S0366: 2, H0144: 2, L0002: 1, S0001: 1, H0619: 1, S0036: 1, L0750: 1 and L0604: 1.		
		1208739	108	213 - 611	295	Ser-50 to His-56.			
		1046466	109	341 - 562	296	Glu-16 to Gln-23, Pro-27 to Gly-34.			
12	HSYIH77	1276392	22	62 - 2551	209	His-61 to Ala-69, Pro-76 to Tyr-85,	L0766: 5, L0779: 5, L0731: 4, S0358: 3,		

						His-98 to Cys-110, Thr-138 to Glu-145, Leu-386 to Glu-394, Glu-403 to Leu-408, Gly-427 to Trp-433, Asp-443 to Leu-450, Phe-462 to Val-469, Arg-513 to Val-520, Met-522 to Arg-527, Arg-560 to Phe-566, Gly-602 to Gly-608, Phe-632 to Asp-638, Leu-649 to Gly-658, Thr-677 to Thr-684, Asn-818 to Leu-826.	L0770: 2, L0794: 2, S0374: 2, L0747: 2, L0749: 2, S0444: 1, H0013: 1, H0575: 1, H0581: 1, H0572: 1, H0354: 1, H0622: 1, H0591: 1, H0551: 1, H0494: 1, S0440: 1, H0529: 1, L0796: 1, L0773: 1, L0662: 1, L0804: 1, L0659: 1, L0790: 1, S0053: 1, H0690: 1, H0648: 1, H0672: 1, S0028: 1, L0780: 1, S0434: 1, S0192: 1, H0543: 1 and H0423: 1.		
		1209388	110	50 - 448	297				
13	HTAHS92	1243918	23	65 - 391	210	Arg-24 to Cys-31, Pro-62 to Thr-73.	H0436: 2, H0556: 1, H0635: 1 and L0789: 1.		
		1213187	111	193 - 519	298	Arg-24 to Cys-31, Pro-62 to Thr-73.			
		1042420	112	25 - 228	299	Lys-6 to Ser-18.			
14	HAROV59	1272018	24	49 - 510	211	Gly-44 to Tyr-50, Pro-66 to Pro-77, Glu-96 to Gly-101, Ser-119 to Glu-136.	H0592: 2		
		1209631	113	39 - 623	300	Gly-44 to Tyr-50,			

						Pro-66 to Pro-77, Glu-96 to Gly-101, Ser-119 to Glu-136, Thr-162 to Leu-167.			
15	HDCCG73	1243884	25	45 - 308	212	Trp-42 to Gly-49.	H0637: 1		
		1209263	114	100 - 363	301	Trp-42 to Gly-49.			
16	HQAHD50	1243837	26	184 - 456	213	Met-1 to Met-6, Pro-10 to Pro-15, Pro-49 to Val-56, Pro-59 to Ser-64, His-66 to Lys-73, Val-75 to Lys-81.	H0696: 1		
		1209703	115	157 - 429	302	Met-1 to Met-6, Pro-10 to Pro-15, Pro-49 to Val-56, Pro-59 to Ser-64, His-66 to Lys-73, Val-75 to Lys-81.			
17	HROBA16	1243878	27	317 - 421	214		H0598: 1		
		1218577	116	342 - 446	303				
		1046802	117	322 - 462	304				
18	HTPJD12	1262048	28	23 - 760	215	Glu-20 to Gly-25, Gly-27 to Trp-34, Gly-173 to Gly-178, Thr-199 to Thr-206, Leu-229 to Lys-242.	S0380: 5, L0748: 4, H0648: 3, S0378: 3, L0752: 3, L0766: 2, L0803: 2, L0665: 2, L0750: 2, H0661: 1, H0461: 1, H0270: 1, H0039: 1, H0622: 1,		

							L0761: 1, L0657: 1, L0532: 1, L0666: 1, H0689: 1, S0330: 1, L0749: 1 and L0777: 1.		
		1209268	118	21 - 758	305	Glu-20 to Gly-25, Gly-27 to Trp-34, Gly-173 to Gly-178, Thr-199 to Thr-206, Leu-229 to Lys-242.			
19	HHAWD13	1272864	29	261 - 1640	216	Asn-45 to Gly-51, Arg-78 to Gly-84, Ser-127 to Glu-156, Asn-167 to Gly-178, Tyr-188 to Asn-193, Arg-242 to Arg-247, Lys-275 to Thr-282.	S0418: 1		
		1209632	119	235 - 654	306	Asn-45 to Gly-51, Arg-78 to Gly-84, Ser-127 to Ser-140.			
20	HISFI83	1243886	30	145 - 477	217	Ile-38 to Leu-51, Tyr-89 to Phe-99.	H0124: 6, L0438: 6, L0758: 6, S0422: 4, L0754: 4, L0766: 3, L0803: 3, L0740: 3, L0779: 3, H0574: 2, L0763: 2, L0565: 2, S0328: 2, L0439: 2, L0777: 2, T0002: 1, H0583: 1, S0442: 1, S0360: 1, H0580: 1,		

							S0132: 1, H0497: 1, H0036: 1, S0382: 1, L0800: 1, L0794: 1, L0774: 1, L0651: 1, L0783: 1, L0790: 1, L0666: 1, L0663: 1, L0665: 1, S0374: 1, H0658: 1, H0539: 1, H0555: 1, L0756: 1, L0731: 1, S0436: 1, S0452: 1 and H0352: 1.		
		1209270	120	287 - 619	307	Ile-38 to Leu-51, Tyr-89 to Phe-99.			
21	HISFV70	1253160	31	71 - 394	218	Thr-18 to Gly-23, His-68 to Gly-90.	H0539: 2, L0752: 2, H0599: 1, S0366: 1, L0639: 1, L0664: 1, H0547: 1, S0330: 1, L0777: 1 and L0604: 1.		
		1209259	121	99 - 422	308	Thr-18 to Gly-23, His-68 to Gly-90.			
22	HNSAB41	1268184	32	221 - 1507	219	Ala-33 to Gly-38, Ser-66 to Pro-76, Pro-149 to Glu-154, Arg-232 to Ala-251, Thr-262 to Asp-267, Ala-350 to Ser-363, Gly-371 to Leu-377, Val-381 to Ser-387, Val-406 to Ala-422.	L0373: 3, L0754: 3, L0005: 2, S0354: 2, H0331: 2, L0157: 2, L0646: 2, L0803: 2, L0659: 2, L0748: 2, S0436: 2, L0581: 2, H0170: 1, S0376: 1, H0574: 1, H0632: 1, H0590: 1, H0596: 1,		

							H0046: 1, H0510: 1, S0214: 1, H0622: 1, H0644: 1, H0598: 1, S0440: 1, H0509: 1, L0598: 1, L0649: 1, S0406: 1, S0434: 1 and L0601: 1.		
		1212804	122	206 - 961	309	Ala-33 to Gly-38, Ser-66 to Pro-76, Pro-149 to Glu-154, Cys-237 to Glu-243.			
23	HOCNY94	1278041	33	100 - 474	220	Pro-34 to Pro-40, Trp-59 to Ser-66, Pro-72 to Leu-77, Pro-79 to Trp-85, Ile-90 to Gly-95, Thr-102 to Gly-110, Asp-118 to Pro-124.	S0358: 2, S0442: 1, S0444: 1, H0550: 1, H0144: 1 and S0152: 1.		
		1209024	123	86 - 460	310	Pro-34 to Pro-40, Trp-59 to Ser-66, Pro-72 to Leu-77.			
24	HAROG72	1281478	34	230 - 490	221	Ala-29 to Val-43, Gly-47 to Arg-56, Arg-62 to Cys-68.	L0809: 4, L0747: 4, H0333: 2, H0716: 1, H0589: 1, S0442: 1, S0300: 1, H0592: 1, H0123: 1, H0024: 1, H0090: 1, L0638: 1, L0637: 1, L0768: 1, L0794: 1, L0766: 1,		

							L0649: 1, L0776: 1, L0657: 1, L0517: 1, L0666: 1, L0663: 1, S0328: 1, H0555: 1, L0750: 1, L0777: 1, L0755: 1, L0731: 1, L0759: 1 and H0422: 1.		
		1209767	124	215 - 478	311	Ala-29 to Val-43, Gly-47 to Arg-56, Arg-62 to Cys-68.			
25	HDACT07	1280454	35	28 - 282	222	Pro-75 to Gln-83.	L0758: 9, L0769: 4, H0556: 3, L0756: 3, H0486: 2, H0156: 2, H0040: 2, H0529: 2, L0766: 2, L0803: 2, L0659: 2, L0809: 2, L0565: 2, L0748: 2, L0754: 2, L0777: 2, H0595: 2, L0595: 2, L0361: 2, S0358: 1, H0580: 1, H0587: 1, H0497: 1, H0013: 1, H0427: 1, H0581: 1, H0251: 1, H0046: 1, H0320: 1, H0594: 1, H0266: 1, H0031: 1, L0055: 1, H0634: 1, S0038: 1, H0100: 1, L0667: 1, L0771: 1,		

							L0804: 1, L0776: 1, L5623: 1, L0791: 1, L0793: 1, L0665: 1, H0547: 1, H0519: 1, S0126: 1, H0682: 1, H0659: 1, H0539: 1, H0521: 1, S0404: 1, L0740: 1, L0747: 1, L0759: 1, S0436: 1 and L0591: 1.		
		1209253	125	513 - 767	312	Pro-75 to Gln-83.			
26	HLTIJ80	1034753	36	111 - 341	223	Asn-31 to Leu-38.	H0591: 1		
		1046031	126	3 - 215	313				
27	HNTZG72	1246154	37	95 - 523	224	Glu-137 to Asp-142.	S0418: 2 and H0547: 1.		
		1209378	127	76 - 504	314	Glu-137 to Asp-142.			
28	HNUCE33	1275160	38	341 - 595	225	Lys-6 to Tyr-11.	L0439: 8, L0777: 6, L0749: 5, L0759: 5, S0360: 4, L0776: 4, L0438: 4, H0670: 4, H0624: 3, L0662: 3, L0803: 3, L0809: 3, S0378: 3, S0406: 3, L0758: 3, S0434: 3, S0442: 2, S0408: 2, H0428: 2, H0644: 2, L0766: 2, L4763: 2, L0666: 2, S0328: 2, H0696: 2, L0751: 2,		

							L0599: 2, S0194: 2, S0196: 2, H0341: 1, H0661: 1, H0580: 1, H0392: 1, H0331: 1, H0427: 1, L0022: 1, H0318: 1, H0263: 1, H0123: 1, S0003: 1, H0615: 1, H0688: 1, H0038: 1, H0040: 1, H0413: 1, H0625: 1, S0438: 1, S0002: 1, S0426: 1, L0369: 1, L0637: 1, L0794: 1, L0650: 1, L0774: 1, L0659: 1, L0792: 1, L0664: 1, H0144: 1, H0697: 1, S0374: 1, H0547: 1, H0690: 1, H0682: 1, H0684: 1, H0659: 1, H0672: 1, H0651: 1, S0332: 1, H0521: 1, H0478: 1, S0390: 1, L0743: 1, L0740: 1, L0754: 1, L0750: 1, L0779: 1, L0752: 1, S0260: 1, H0445: 1, L0485: 1, L0608: 1, S0242: 1 and H0543: 1.		

		1209149	128	2743 - 2997	315	Lys-6 to Tyr-11.			
29	HODEM32	1253127	39	399 - 665	226	His-24 to Phe-32, Pro-59 to Gln-69.	H0615: 1		
		1212873	129	387 - 653	316	His-24 to Phe-32.			
30	HPJHQ20	1261918	40	70 - 453	227	Trp-61 to Thr-67, Ile-73 to Ser-84, Ser-87 to Ile-92.	S0152: 1		
		1209298	130	57 - 440	317	Trp-61 to Thr-67, Ile-73 to Ser-84, Ser-87 to Ile-92.			
31	HQADO95	1276422	41	122 - 373	228	Pro-44 to Gln-49, Pro-52 to Ser-60.	H0156: 1, H0696: 1 and H0352: 1.		
		1209746	131	107 - 358	318	Pro-44 to Gln-49, Pro-52 to Ser-60.			
32	HTENS88	1243927	42	233 - 577	229	Gln-27 to Ser-33, Thr-71 to Thr-80, Val-83 to Ser-98.	L0766: 13, S0422: 8, H0014: 2, S0440: 2, H0529: 2, L0751: 2, H0661: 1, H0637: 1, L0717: 1, H0587: 1, H0497: 1, H0486: 1, H0581: 1, H0052: 1, L0157: 1, S0003: 1, H0616: 1, L0598: 1, L0643: 1, L0768: 1, L0776: 1, L0663: 1, L0664: 1, H0144: 1, H0690: 1, H0670: 1, S0330: 1, S0380: 1,		

							S0152: 1, S0404: 1, L0756: 1, L0779: 1, L0758: 1, S0308: 1, S0192: 1, H0422: 1, S0412: 1 and S0424: 1.		
		1213009	132	226 - 483	319	Gln-27 to Ser-33.			
		1045824	133	1 - 210	320				
33	HTLGC03	1261928	43	264 - 509	230	Gly-16 to Ala-22, Ala-54 to Ala-62, Ser-69 to Ser-81.	AR052: 14, AR055: 10, AR060: 7, AR089: 6, AR053: 6, AR061: 6, AR033: 5, AR096: 5, AR039: 3, AR104: 3 H0556: 4, L0646: 4, L0794: 4, H0253: 3, L0758: 3, H0618: 2, H0038: 2, H0040: 2, L0764: 2, L0776: 2, L0807: 2, L0809: 2, L0439: 2, L0751: 2, S0040: 1, H0341: 1, S0360: 1, H0734: 1, H0156: 1, H0309: 1, H0231: 1, H0012: 1, H0057: 1, H0355: 1, H0163: 1, H0090: 1, H0551: 1, S0038: 1, H0100: 1, L0640: 1, L0371: 1, L0667: 1,		

							L0648: 1, L0768: 1, L0803: 1, L0806: 1, L0659: 1, L0789: 1, L0665: 1, H0690: 1, H0658: 1, H0672: 1, S0330: 1, S0406: 1, L0731: 1, L0757: 1, S0434: 1, S0436: 1, L0593: 1, H0422: 1, S0424: 1 and H0008: 1.		
		1212925	134	257 - 502	321	Gly-16 to Ala-22.			
		1227183	135	2109 - 2117	322				
34	HTLKQ55	1243896	44	261 - 1082	231	Glu-37 to Val-43, Gln-229 to Tyr-240, Asp-250 to Gln-260.	H0618: 3 and H0253: 1.		
		1213423	136	249 - 665	323	Glu-37 to Val-43.			
35	HTOJF42	1261944	45	96 - 434	232		H0656: 1, H0255: 1, H0264: 1, H0131: 1 and L0644: 1.		
		1213137	137	91 - 462	324				
36	HTPHC19	1284768	46	225 - 473	233	Ser-38 to Ser-44, Gly-67 to Lys-72.	L0547: 2, H0635: 1, H0622: 1, L0475: 1, H0727: 1 and H0721: 1.		
		1212930	138	397 - 645	325	Ser-38 to Ser-44.			
37	HDPHG50	1268191	47	200 - 610	234	Gln-68 to Gly-73, Pro-99 to Ala-120, Asp-126 to Ser-136.	L0805: 3, H0521: 2, H0735: 1, S0386: 1, L0776: 1, L0438: 1, H0478: 1, L0439: 1 and		

							S0436: 1.		
		1213570	139	205 - 948	326				
		1144654	140	2773 - 2856	327				
38	HHEWS13	1243859	48	420 - 563	235	Thr-40 to Glu-47.	H0543: 1		
		1209615	141	410 - 565	328	Tyr-40 to Ser-46.			
39	HOGCY01	1209803	49	141 - 506	236	Asn-12 to Lys-19.	H0402: 2, L0766: 2, L0659: 2, S0212: 1, S0356: 1, L0769: 1, L5575: 1, L0800: 1, L0764: 1, L0794: 1, L0809: 1, L0789: 1, L4559: 1, L0438: 1, H0435: 1, L0439: 1 and L0758: 1.		
40	HPJGT38	1209290	50	6 - 278	237	Gln-59 to Pro-67.			
41	HTFMK11	1276752	51	429 - 530	238		H0624: 1, S0050: 1, S0051: 1, L0805: 1, L0748: 1, L0755: 1, L0588: 1 and S0424: 1.		
		1212928	142	476 - 577	329				
		1042907	143	3 - 299	330				
42	HTSGQ95	1280458	52	88 - 195	239		H0521: 6, H0587: 2, H0087: 2, S0404: 2, H0685: 1, H0657: 1, H0661: 1, H0580: 1, S0222: 1, H0592: 1, L0483: 1, H0628: 1, H0129: 1, S0144: 1,		

							H0529: 1, L0761: 1, L0766: 1, L0774: 1, L0657: 1, L0791: 1, L0793: 1, H0698: 1, L0438: 1, H0547: 1, L0731: 1, S0436: 1 and H0543: 1.		
		1213625	144	88 - 195	331				
		1226328	145	1153 - 1938	332	Gln-11 to Gln-17, Glu-68 to Gly-81, Ala-111 to Ala-117, Gly-146 to Gln-153.			
43	HLSAI43	1243888	53	191 - 439	240	Lys-36 to Arg-41, Gly-53 to Asp-67.	H0306: 1 and H0540: 1.		
		1213409	146	181 - 429	333	Lys-36 to Arg-41, Gly-53 to Asp-67.			
44	HNBTF02	1253163	54	32 - 691	241	Pro-49 to Pro-70, Gly-115 to Ser-121, Ala-133 to Arg-138, Glu-168 to Phe-175.	L0758: 7, L0666: 5, L0749: 4, L0779: 4, H0620: 3, L0540: 3, L0439: 3, L0750: 3, L0731: 3, L0759: 3, S0360: 2, L0763: 2, L0770: 2, L0803: 2, L0775: 2, L0805: 2, L0776: 2, L0665: 2, L0743: 2, L0747: 2, L0756: 2, S0040: 1, H0662: 1, S0045: 1,		

							H0549: 1, H0550: 1, H0370: 1, T0060: 1, L0022: 1, H0572: 1, H0615: 1, H0135: 1, H0488: 1, H0623: 1, H0059: 1, H0022: 1, L0520: 1, L0640: 1, L0769: 1, L0772: 1, L0662: 1, L0768: 1, L0766: 1, L0804: 1, L0774: 1, L0655: 1, L0809: 1, L4501: 1, L0663: 1, L0664: 1, H0144: 1, H0547: 1, S0330: 1, H0539: 1, H0696: 1, L0744: 1, L0748: 1, L0751: 1 and L0757: 1.		
		1226356	147	154 - 1917	334	Pro-49 to Pro-70, Gly-115 to Ser-121, Ala-133 to Arg-138, Glu-168 to Phe-175, Pro-276 to Val-282, Thr-297 to Asp-305, Thr-403 to Gly-408, Ser-494 to Gln-502, Pro-539 to Arg-547.			
45	HNSCC06	1263307	55	25 - 570	242	Ala-60 to Trp-66, Lys-86 to His-99,	L0766: 2, H0265: 1, H0717: 1, S0046: 1,		

						Asp-104 to Leu-111.	H0574: 1, H0590: 1, H0581: 1, H0594: 1, H0031: 1, H0090: 1, H0264: 1, L0774: 1, H0519: 1, H0435: 1, S0152: 1, L0752: 1, S0434: 1 and H0677: 1.		
		1209025	148	8 - 1021	335	Ala-60 to Trp-66, Lys-86 to His-99, Asp-104 to Leu-111.			
46	HTENQ40	1243926	56	84 - 461	243	Ser-75 to Met-81.	H0616: 1		
		1213048	149	77 - 454	336	Ser-75 to Met-81.			
47	HCNCM78	1243864	57	34 - 432	244	Thr-22 to Cys-40, Val-44 to Asn-51, Pro-72 to Pro-81, His-93 to His-99, Gln-112 to Ser-117, Thr-120 to Cys-132.	L0771: 9, S0358: 7, L0764: 5, S0374: 3, L0751: 3, H0597: 2, L0804: 2, L0806: 2, L0789: 2, S0406: 2, S0442: 1, S0354: 1, S0444: 1, S0408: 1, H0587: 1, H0232: 1, L0738: 1, H0512: 1, S0440: 1, L0773: 1, L4500: 1, L0803: 1, L0664: 1, S0330: 1 and S0044: 1.		
		1225879	150	24 - 422	337	Thr-22 to Cys-40, Val-44 to Asn-51, Pro-72 to Pro-81,			

						His-93 to His-99, Gln-112 to Ser-117, Thr-120 to Cys-132.			
		1225880	151	55 - 300	338	Thr-22 to Cys-40, Val-44 to His-56.			
48	HCOKD57	1271607	58	64 - 624	245	Ser-37 to Thr-42, Cys-66 to Ser-71, Cys-87 to Asp-101, Ile-142 to Thr-149, Cys-176 to His-184.	AR039: 8, AR053: 6, AR089: 5, AR033: 5, AR052: 5, AR060: 4, AR096: 4, AR055: 3, AR104: 3, AR061: 3 L0750: 5, L0777: 4, L0776: 2, S0406: 2, L0751: 2, L0747: 2, L0758: 2, H0159: 1, H0294: 1, S0114: 1, H0636: 1, H0489: 1, S0007: 1, H0619: 1, H0431: 1, L0251: 1, T0114: 1, H0013: 1, H0327: 1, H0009: 1, H0012: 1, H0083: 1, S0003: 1, H0039: 1, H0598: 1, S0344: 1, S0422: 1, L0769: 1, L0764: 1, L0768: 1, L0775: 1, L0512: 1, L0783: 1, S0428: 1, S0126: 1, H0659: 1, H0648: 1, L0779: 1,		

							L0752: 1, L0731: 1, L0757: 1 and H0667: 1.		
		1213043	152	54 - 575	339	Ser-37 to Thr-42, Cys-66 to Ser-71, Cys-87 to Asp-101, Thr-122 to Thr-127.			
49	HRAEO74	1209635	59	545 - 889	246	Asp-42 to Glu-52, Asp-103 to Ser-114.	H0617: 7, L0771: 6, S0408: 4, S0358: 3, H0638: 2, L0761: 2, L0764: 2, L0655: 2, L0634: 2, L0666: 2, H0435: 2, L0751: 2, L0777: 2, H0506: 2, H0650: 1, H0254: 1, H0255: 1, S0444: 1, H0351: 1, H0549: 1, H0600: 1, H0592: 1, L0022: 1, H0744: 1, H0204: 1, H0231: 1, S0440: 1, L0800: 1, L0643: 1, L0648: 1, L0662: 1, L0776: 1, L0664: 1, S0216: 1, H0690: 1, H0672: 1, S0378: 1, S0406: 1, H0555: 1, L0747: 1 and S0436: 1.		
50	HTACM88	1253076	60	64 - 339	247	Pro-45 to Ala-54.	H0271: 14, L0757: 9, S0428: 5, L0659: 4,		

							S0216: 4, L0751: 4, S0360: 3, L0776: 3, H0416: 2, H0068: 2, L0763: 2, L0772: 2, L0764: 2, L0662: 2, L0775: 2, L0438: 2, H0521: 2, H0671: 1, H0638: 1, S0442: 1, S0408: 1, T0039: 1, H0069: 1, H0635: 1, H0581: 1, H0421: 1, H0719: 1, L0483: 1, L0055: 1, H0634: 1, H0413: 1, L0646: 1, L0642: 1, L0773: 1, L0806: 1, L0789: 1, L0666: 1, S0052: 1, S0053: 1, H0689: 1, H0690: 1, H0518: 1 and L0439: 1.		
		1213431	153	64 - 339	340	Pro-45 to Ala-54.			
		1228352	154	332 - 748	341				
51	HBWBI44	1277904	61	39 - 257	248		S0386: 1 and L0776: 1.		
		1159379	155	425 - 682	342				
52	HAGIF61	1243855	62	160 - 516	249	Ser-29 to Pro-43, Phe-55 to Gln-66, Thr-86 to His-93.	L0747: 7, L0761: 6, H0052: 5, S0358: 4, S0360: 4, L0752: 3, L0592: 3, L0411: 2,		

							L0639: 2, L0627: 2, L0803: 2, L0805: 2, L0664: 2, L0665: 2, S0328: 2, H0710: 2, L0605: 2, H0423: 2, H0556: 1, H0583: 1, S0116: 1, H0663: 1, S0354: 1, H0340: 1, T0114: 1, T0109: 1, L0021: 1, S0346: 1, H0194: 1, H0251: 1, T0010: 1, S0022: 1, H0135: 1, H0494: 1, H0646: 1, H0649: 1, L0373: 1, L0646: 1, L0662: 1, L0794: 1, L0766: 1, L0649: 1, L0775: 1, L0651: 1, L0806: 1, L0659: 1, H0144: 1, H0539: 1, H0521: 1, H0436: 1, L0742: 1, L0740: 1, L0757: 1, H0542: 1, H0008: 1 and H0352: 1.		
		1212943	156	1015 - 1371	343	Ser-29 to Pro-43, Phe-55 to Gln-66, Thr-86 to His-93.			
53	HSYHD12	1280343	63	301 - 1701	250	Gly-22 to Ile-34, Ser-58 to Gly-67,	L0805: 2, H0520: 2, L0748: 2, H0171: 1,		

						Ala-77 to Thr-83, Tyr-104 to Leu-110, Val-132 to Leu-141, Lys-181 to Leu-189, Thr-193 to Lys-198, Glu-242 to Asn-249, Gly-258 to Lys-263, Asn-293 to Ser-303, Arg-308 to Arg-316, His-397 to Lys-406, Ala-425 to Lys-434, Glu-441 to Gly-449, Gln-461 to Leu-466.	H0176: 1, S0360: 1, H0013: 1, H0309: 1, H0046: 1, H0050: 1, H0292: 1, S0003: 1, S0214: 1, H0551: 1, H0647: 1, H0547: 1, H0660: 1, L0777: 1, L0591: 1 and L0608: 1.		
		1209769	157	312 - 1409	344	Gly-22 to Ile-34, Ser-58 to Gly-67, Ala-77 to Thr-83, Tyr-104 to Leu-110, Val-132 to Leu-141, Lys-181 to Ser-188.			
54	HTAGF12	1276746	64	305 - 493	251		H0556: 2, H0635: 2, S0116: 1, S0388: 1, H0634: 1, L0638: 1 and S0031: 1.		
		1222310	158	298 - 486	345				
		1222309	159	28 - 84	346				
55	HTHCA16	1243880	65	77 - 997	252	Gly-59 to Gly-64, Arg-87 to Ser-92, Pro-132 to Gly-137,	H0046: 3, H0341: 2, H0635: 2, H0445: 2, H0295: 1, S0114: 1,		

						Arg-175 to Arg-195, Pro-230 to Trp-236, Gly-277 to Gly-284, Pro-291 to Arg-297.	H0255: 1, S0418: 1, S0007: 1, S0045: 1, H0608: 1, H0587: 1, H0250: 1, S0182: 1, H0052: 1, H0050: 1, H0083: 1, H0266: 1, H0553: 1, H0063: 1, H0264: 1, H0022: 1, S0002: 1, L0763: 1, L0761: 1, L0768: 1, L0794: 1, L0809: 1, S0374: 1, H0689: 1, H0522: 1 and H0423: 1.		
		1059497	160	99 - 1019	347	Gly-59 to Gly-64, Arg-87 to Ser-92, Pro-132 to Gly-137, Arg-175 to Arg-195, Pro-230 to Trp-236, Gly-277 to Gly-284, Pro-291 to Arg-297.			
56	HNFIQ15	1282887	66	105 - 680	253	Ser-4 to Gln-10, Pro-85 to Gly-90, Gly-137 to Gly-146, Arg-154 to Ser-161, Glu-164 to Leu-171, Pro-178 to Glu-190.	H0271: 35, H0253: 29, H0618: 26, L0766: 19, L0769: 12, H0457: 10, S0474: 9, L0731: 9, L0757: 9, L0758: 6, H0445: 6, L0601: 6, S0046: 5, H0179: 5, H0416: 5, S0126: 5, H0265: 4, S0418: 4,		

							S0420: 4, H0069: 4, L0761: 4, L0752: 4, H0556: 3, H0619: 3, H0486: 3, H0052: 3, H0024: 3, H0634: 3, H0623: 3, T0041: 3, L0637: 3, S0006: 3, S0052: 3, L0743: 3, L0754: 3, L0750: 3, H0716: 2, H0255: 2, H0306: 2, H0402: 2, H0592: 2, H0581: 2, H0545: 2, H0046: 2, H0050: 2, H0266: 2, H0622: 2, H0553: 2, S0036: 2, H0087: 2, H0056: 2, L0774: 2, L0655: 2, L0783: 2, L5623: 2, H0547: 2, H0519: 2, L0748: 2, L0751: 2, L0747: 2, L0779: 2, S0436: 2, L0603: 2, H0624: 1, H0171: 1, H0222: 1, H0686: 1, S0040: 1, H0717: 1, H0295: 1, H0657: 1, L0427: 1, H0254: 1, S0358: 1, H0580: 1, H0730: 1,		

							H0437: 1, H0261: 1, S0222: 1, H0610: 1, H0013: 1, H0250: 1, H0002: 1, H0599: 1, H0318: 1, H0086: 1, H0567: 1, H0123: 1, H0015: 1, T0010: 1, H0355: 1, H0286: 1, S0250: 1, H0031: 1, H0628: 1, H0135: 1, H0090: 1, H0551: 1, H0264: 1, H0412: 1, H0413: 1, H0100: 1, H0494: 1, S0438: 1, S0144: 1, S0002: 1, L0770: 1, L5575: 1, L0667: 1, L0772: 1, L0646: 1, L0662: 1, L0794: 1, L0387: 1, L0775: 1, L0653: 1, L0659: 1, L0809: 1, L0789: 1, L0792: 1, L0663: 1, L0665: 1, S0428: 1, S0216: 1, L0565: 1, H0435: 1, H0658: 1, S0380: 1, S0152: 1, S0190: 1, H0134: 1, H0555: 1, H0436: 1, S0390: 1,		

							S0037: 1, L0439: 1, H0707: 1, S0194: 1, S0196: 1, H0542: 1, H0543: 1 and H0422: 1.		
		1212720	161	105 - 425	348	Ser-4 to Gln-10, Pro-85 to Val-91.			
		1201579	162	417 - 827	349	Ser-4 to Ala-14, Ala-43 to Cys-56, Pro-92 to Thr-97.			
		1049987	163	255 - 560	350	Glu-1 to Pro-10.			
57	HNHPS28	1243890	67	208 - 648	254	Glu-18 to Lys-34, Ser-41 to Ser-56, Gly-61 to Lys-67, Met-77 to Gly-82, Glu-89 to His-96.	S0216: 1		
		1209276	164	201 - 599	351	Glu-18 to Lys-34, Ser-41 to Ser-56, Gly-61 to Lys-67, Met-77 to Gly-82, Glu-89 to His-96.			
58	HNTDN59	1280527	68	117 - 2450	255	Pro-25 to Val-31, Trp-157 to Thr-167, Ala-311 to Arg-318, Ser-354 to Phe-361, Cys-377 to Met-383, Asn-389 to Lys-395, Pro-407 to Asp-414, Glu-421 to Asn-430,	L0744: 15, L0758: 15, L0747: 13, S0358: 12, H0539: 12, L0439: 12, L0766: 10, L0770: 9, L0750: 9, H0574: 8, L0775: 8, L0748: 7, L0646: 6, L0666: 6, L0752: 6, S0442: 5,		

						Asp-433 to Ile-438, Gln-465 to Thr-472, Val-475 to Leu-480, Asp-492 to Asp-498, Pro-527 to Glu-533, Ser-670 to Lys-675, Thr-734 to Arg-740.	H0632: 5, H0551: 5, L0769: 5, L0659: 5, L0519: 5, L0755: 5, S0360: 4, S0007: 4, H0046: 4, H0012: 4, H0510: 4, S0440: 4, L0764: 4, H0521: 4, L0759: 4, H0657: 3, S0420: 3, S0046: 3, H0441: 3, H0486: 3, H0575: 3, H0327: 3, H0544: 3, H0620: 3, H0687: 3, H0617: 3, H0413: 3, L0774: 3, L0776: 3, L0657: 3, L0664: 3, L0665: 3, S0374: 3, S0328: 3, S0152: 3, S0406: 3, S3012: 3, L0751: 3, L0754: 3, L0777: 3, L0591: 3, H0624: 2, H0170: 2, H0556: 2, S0134: 2, H0583: 2, S0354: 2, S0410: 2, H0393: 2, H0549: 2, S0222: 2, H0331: 2, H0492: 2, S0280: 2, H0599: 2, H0036: 2, H0421: 2, H0309: 2,		

							H0009: 2, H0051: 2, H0083: 2, H0181: 2, H0674: 2, H0400: 2, H0412: 2, S0038: 2, H0100: 2, H0494: 2, S0438: 2, H0509: 2, S0150: 2, S0002: 2, L0637: 2, L0771: 2, L0662: 2, L0768: 2, L0794: 2, L0803: 2, L0804: 2, L0375: 2, L0651: 2, L0806: 2, L0655: 2, L0791: 2, H0593: 2, H0660: 2, H0522: 2, L0731: 2, L0485: 2, L0581: 2, L0608: 2, L0593: 2, L0594: 2, L0361: 2, S0194: 2, H0149: 1, H0265: 1, S0040: 1, S6024: 1, T0049: 1, L0785: 1, H0484: 1, H0255: 1, H0662: 1, H0638: 1, S0418: 1, S0376: 1, S0444: 1, S0408: 1, S0300: 1, H0411: 1, S0278: 1, H0431: 1, H0409: 1, H0586: 1, H0333: 1,		

							L0622: 1, H0485: 1, T0040: 1, H0635: 1, H0156: 1, H0042: 1, S0010: 1, T0048: 1, H0052: 1, H0251: 1, H0263: 1, H0596: 1, T0115: 1, T0110: 1, L0040: 1, H0545: 1, H0041: 1, H0123: 1, H0011: 1, H0024: 1, L0163: 1, S0051: 1, H0355: 1, S0314: 1, H0252: 1, L0483: 1, H0424: 1, H0213: 1, H0031: 1, H0673: 1, S0364: 1, L0456: 1, H0598: 1, H0135: 1, H0087: 1, H0272: 1, H0488: 1, H0433: 1, H0625: 1, H0386: 1, H0647: 1, S0142: 1, S0210: 1, S0422: 1, S0426: 1, H0529: 1, L0371: 1, L0761: 1, L0772: 1, L0641: 1, L0374: 1, L0649: 1, L0381: 1, L0650: 1, L0526: 1, L0518: 1, L0782: 1, L0783: 1,		

							L0382: 1, L0809: 1, L0647: 1, L0790: 1, L0793: 1, L0663: 1, H0144: 1, H0547: 1, H0519: 1, S0126: 1, H0711: 1, H0690: 1, H0682: 1, H0435: 1, H0659: 1, H0658: 1, H0670: 1, S0378: 1, S0380: 1, H0710: 1, S0013: 1, H0696: 1, H0704: 1, S0044: 1, S3014: 1, S0028: 1, L0743: 1, L0740: 1, L0756: 1, L0779: 1, L0780: 1, L0757: 1, H0445: 1, L0588: 1, S0011: 1, S0026: 1, H0136: 1, S0276: 1, H0422: 1, S0462: 1 and H0506: 1.		
l		1215793	165	106 - 516	352	Pro-25 to Val-31.			
l		1215794	166	107 - 508	353	Pro-25 to Val-31.			
		1210379	167	1 - 909	354	Lys-53 to Asn-58, Thr-282 to Gly-288, Glu-294 to Gln-303.			
59	HNTQM17	1283173	69	251 - 904	256	Pro-69 to Gln-75, Arg-81 to Leu-90, Glu-119 to Tyr-124,	L0803: 4, L0439: 4, L0774: 3, L0777: 3, S0212: 2, H0169: 2,		

						Lys-178 to Glu-184, Leu-201 to Asn-206, Leu-210 to Gly-215.	L0805: 2, H0354: 1, T0006: 1, H0553: 1, L0770: 1, L0639: 1, L0764: 1, L0794: 1, L0804: 1, L0378: 1, L0783: 1, L0789: 1, H0519: 1, L0748: 1, L0749: 1 and L0758: 1.		
		1209252	168	241 - 594	355				
60	HNTTF76	1243907	70	59 - 340	257	Thr-32 to Ser-38, Thr-46 to Pro-51.	H0556: 1 and H0547: 1.		
		1213468	169	48 - 329	356	Thr-32 to Ser-38, Thr-46 to Pro-51.			
61	HCFGD60	1253155	71	137 - 505	258	Ser-97 to Trp-104.	L0794: 2, L0439: 2, S0354: 1, S0002: 1, L0779: 1, H0445: 1 and H0422: 1.		
		1212775	170	496 - 864	357	Ser-97 to Trp-104.			
62	HMUEP30	1262057	72	251 - 592	259	Pro-6 to Trp-12, Thr-18 to Pro-24, Pro-47 to Trp-63, Pro-71 to Phe-76, Pro-99 to Trp-111.	H0529: 8, L0794: 5, S0424: 4, H0559: 3, H0083: 3, L0769: 3, L0809: 3, L0748: 3, L0759: 3, S0192: 3, H0341: 2, H0587: 2, H0266: 2, H0286: 2, H0623: 2, S0422: 2, L0761: 2, L0783: 2, L0565: 2, L0745: 2,		

							L0756: 2, L0777: 2, H0665: 2, H0739: 1, H0265: 1, H0685: 1, H0657: 1, H0484: 1, S0420: 1, S0358: 1, H0592: 1, H0013: 1, H0427: 1, L0021: 1, S0474: 1, H0581: 1, H0597: 1, H0546: 1, H0046: 1, H0086: 1, H0024: 1, H0604: 1, H0181: 1, H0272: 1, S0438: 1, H0647: 1, S0144: 1, L0639: 1, L0372: 1, L0800: 1, L0644: 1, L0766: 1, L0803: 1, L0382: 1, L0787: 1, L0788: 1, L0663: 1, S0374: 1, H0547: 1, H0593: 1, H0521: 1, H0522: 1, S3014: 1, S0027: 1, L0740: 1, L0751: 1, L0746: 1, L0749: 1, L0779: 1, L0757: 1 and S0436: 1.		
		1209865	171	241 - 528	358	Pro-6 to Trp-12, Thr-18 to Pro-24, Pro-47 to Trp-63,			

						Pro-71 to Phe-76.			
63	HNSCA10	1268201	73	279 - 926	260	Met-1 to Lys-6, Met-170 to His-176, Lys-207 to Glu-215.	L0777: 8, L0749: 4, S0434: 4, H0551: 3, S0026: 3, S0010: 2, L0748: 2, L0751: 2, L0750: 2, L0759: 2, S0358: 1, S0408: 1, L0021: 1, T0082: 1, T0010: 1, H0083: 1, L0483: 1, L0455: 1, H0616: 1, H0494: 1, H0560: 1, H0529: 1, L0646: 1, L0641: 1, L0643: 1, L0662: 1, L0775: 1, L0661: 1, L0526: 1, L0789: 1, S0374: 1, H0547: 1, H0519: 1, S0126: 1, S0378: 1, L0740: 1, L0747: 1, L0592: 1 and S0242: 1.		
		1209403	172	266 - 652	359	Met-1 to Lys-6.			
64	HTPAO67	1280558	74	2709 - 2963	261	Met-1 to Lys-10, Leu-30 to Thr-42.	L0748: 6, L0747: 6, S0360: 5, L0777: 5, L0731: 5, L0599: 5, H0486: 4, H0644: 4, L0588: 4, H0013: 3, H0599: 3, H0575: 3, H0622: 3, H0412: 3,		

							H0413: 3, H0056: 3, L0769: 3, L0803: 3, L0805: 3, L0439: 3, L0749: 3, S0116: 2, H0375: 2, H0032: 2, H0674: 2, H0038: 2, H0623: 2, L0770: 2, L0646: 2, L0807: 2, L0809: 2, L0789: 2, L0744: 2, L0752: 2, H0595: 2, L0605: 2, L0604: 2, H0624: 1, H0717: 1, H0716: 1, S0282: 1, H0661: 1, H0638: 1, S0442: 1, S0444: 1, H0208: 1, H0437: 1, H0431: 1, H0601: 1, T0060: 1, H0069: 1, H0427: 1, L0022: 1, S0474: 1, H0235: 1, H0050: 1, H0197: 1, H0024: 1, H0266: 1, H0271: 1, H0039: 1, L0143: 1, H0111: 1, H0634: 1, H0616: 1, H0268: 1, H0509: 1, H0647: 1, S0422: 1, L0640: 1, L0637: 1, L0768: 1,		

							L0775: 1, L0659: 1, L0666: 1, L0665: 1, H0144: 1, S0126: 1, H0689: 1, H0682: 1, H0659: 1, H0672: 1, S0406: 1, H0727: 1, S0206: 1, L0780: 1, L0581: 1 and H0506: 1.		
		1217178	173	1579 - 1833	360	Met-1 to Lys-10, Leu-30 to Thr-42.			
		1217177	174	6 - 269	361	Val-4 to Gln-10.			
65	HAZCB15	1243853	75	32 - 382	262	Asp-33 to Gly-43, Ser-54 to His-60, Pro-111 to Phe-116.	H0690: 1		
		1209801	175	7 - 357	362				
66	HSLFK66	1271609	76	167 - 586	263	Lys-133 to Asp-139.	S0028: 19, S0031: 9, S0052: 8, S0050: 7, L0105: 5, S0282: 4, H0381: 3, S0045: 3, S0278: 3, H0271: 3, H0617: 3, S0428: 3, S0001: 2, S0049: 2, H0196: 2, H0179: 2, S0038: 2, S0144: 2, S0044: 2, S0390: 2, S0206: 2, S0260: 2, L0591: 2, L0362: 2, L0361: 2, L0603: 2,		

							S0035: 1, S0046: 1, H0253: 1, H0318: 1, T0110: 1, H0266: 1, H0416: 1, H0031: 1, H0180: 1, H0181: 1, H0383: 1, H0169: 1, S0036: 1, H0135: 1, H0163: 1, H0634: 1, H0164: 1, L0374: 1, L0379: 1, S0126: 1, S0037: 1 and S3014: 1.		
		1224406	176	2610 - 3029	363	Lys-133 to Asp-139.			
67	HCFPE46	1243901	77	151 - 399	264		H0728: 1, H0734: 1, H0708: 1, H0494: 1, L0665: 1, H0672: 1, H0694: 1 and H0423: 1.		
		1223989	177	140 - 388	364				
68	HNGPB91	1253113	78	83 - 262	265		S0428: 1		
		1212875	178	70 - 249	365				
		1045322	179	111 - 413	366				
69	HRADV31	1275159	79	203 - 298	266		L0439: 6, L0748: 2, L0756: 2, L0779: 2, L0758: 2, L0608: 2, H0624: 1, S0001: 1, S0442: 1, S0360: 1, H0619: 1, L0717: 1, H0486: 1, H0596: 1, L0041: 1, L0471: 1,		

							H0032: 1, H0591: 1, L0351: 1, H0494: 1, H0561: 1, L0764: 1, L0766: 1, L0803: 1, L0774: 1, L0651: 1, L0629: 1, L0665: 1, L0438: 1, H0555: 1, H0436: 1, L0740: 1, L0777: 1, L0759: 1, L0605: 1 and S0242: 1.		
l		1209606	180	188 - 283	367				
		1046790	181	54 - 407	368				
70	HNBVG70	1243889	80	273 - 536	267	Asp-10 to Ala-17, Arg-75 to Glu-81.	L0439: 4, L0794: 3, L0803: 3, L0805: 3, H0662: 2, L0769: 2, L0776: 2, L0438: 2, L0744: 2, L0748: 2, L0599: 2, S6024: 1, S0360: 1, H0411: 1, S0222: 1, H0592: 1, H0587: 1, L0021: 1, H0688: 1, L0455: 1, S0366: 1, H0616: 1, H0551: 1, L0764: 1, L0804: 1, L0787: 1, L0663: 1, L0745: 1, L0779: 1, L0758: 1 and S0436: 1.		
		1225912	182	981 - 1244	369	Pro-11 to Ala-17,			

						Arg-75 to Glu-81.			
71	HCFGK19	1253156	81	334 - 555	268		S0114: 1, H0305: 1 and H0422: 1.		
		1213458	183	472 - 693	370				
72	HNGOG04	1243925	82	27 - 272	269	Arg-22 to Leu-30.	S0428: 1		
		1212831	184	20 - 265	371	Arg-22 to Leu-30.			
73	HDCGC29	1253157	83	269 - 424	270	Met-1 to Val-6.	H0637: 1		
		1210197	185	253 - 435	372				
74	HNGNT27	1261927	84	61 - 312	271	Ser-28 to Ser-38, Cys-51 to Pro-57, Val-60 to Val-65, Arg-67 to Val-78.	S0428: 1		
		1213013	186	54 - 305	373	Ser-28 to Ser-38, Cys-51 to Pro-57, Val-60 to Val-65, Arg-67 to Val-78.			
75	HMUHD72	1281806	85	168 - 422	272	Met-34 to Ser-40, Pro-65 to Ser-83.	H0069: 4, H0599: 4, H0521: 3, L0596: 3, H0341: 2, H0255: 2, H0551: 2, S0344: 2, S0040: 1, H0254: 1, H0125: 1, S0442: 1, H0728: 1, H0208: 1, S0045: 1, S0046: 1, H0437: 1, H0586: 1, H0486: 1, T0114: 1, H0036: 1, H0052: 1, H0327: 1, T0010: 1,		

							H0266: 1, H0288: 1, H0598: 1, H0063: 1, H0488: 1, H0413: 1, S0144: 1, H0529: 1, L0771: 1, L0766: 1, H0555: 1, S0037: 1, S0027: 1, L0439: 1, L0740: 1 and L0366: 1.		
		1209710	187	204 - 458	374	Met-34 to Ser-40, Pro-65 to Ser-83.			
76	HLYCK47	1272921	86	72 - 764	273	Arg-25 to Gly-31, Pro-45 to Gly-52, Pro-71 to Gly-76, Pro-81 to Gly-88, Met-90 to Phe-103, Thr-110 to Pro-119, Pro-132 to Gly-141, Gly-179 to Asn-188.	H0521: 38, H0522: 13, H0445: 6, L0748: 4, S0360: 3, H0264: 3, S0354: 2, H0039: 2, H0622: 2, H0063: 2, S0374: 2, L0744: 2, S0212: 1, S0358: 1, H0427: 1, H0575: 1, H0122: 1, H0309: 1, H0570: 1, H0123: 1, H0620: 1, H0375: 1, H0553: 1, H0644: 1, H0376: 1, L0435: 1, L0439: 1, L0754: 1, S0434: 1, S0106: 1, H0668: 1 and S0384: 1.		
		1221159	188	119 - 550	375	Arg-25 to Gly-31, Pro-45 to Gly-52, Pro-71 to Gly-76,			

						Pro-81 to Gly-91.			
		1221167	189	108 - 845	376	Arg-25 to Gly-31, Pro-45 to Gly-52, Pro-71 to Gly-76, Pro-81 to Gly-91, Glu-107 to Phe-118, Thr-125 to Pro-134, Pro-147 to Gly-156, Gly-194 to Asn-203.			
77	HLYFJ90	1243873	87	230 - 481	274	Arg-50 to Leu-60.	L0749: 5, L0769: 4, L0758: 4, L0731: 3, L0804: 2, L0774: 2, L0757: 2, H0662: 1, S0358: 1, S0444: 1, S0222: 1, H0441: 1, L0623: 1, H0251: 1, H0046: 1, H0569: 1, H0673: 1, H0494: 1, L0763: 1, L0764: 1, L0662: 1, L0794: 1, L0375: 1, L0806: 1, L0805: 1, L0532: 1, H0593: 1, H0539: 1, L0742: 1, L0748: 1, L0747: 1, L0750: 1, L0779: 1, L0777: 1 and H0445: 1.		
		1218626	190	258 - 509	377	Arg-50 to Leu-60.			
78	HMLHD54	1243834	88	75 - 350	275	Met-1 to Leu-6,	L0665: 5, L0777: 5,		

						Thr-32 to Glu-39.	H0521: 4, S0026: 4, L0662: 3, H0520: 3, L0596: 3, L0592: 3, H0632: 2, H0012: 2, H0266: 2, H0264: 2, L0773: 2, L0774: 2, L0659: 2, L0663: 2, L0664: 2, S0126: 2, H0684: 2, L0748: 2, L0779: 2, L0752: 2, H0506: 2, H0686: 1, H0717: 1, H0716: 1, L0778: 1, S0116: 1, S0212: 1, H0638: 1, S0356: 1, S0442: 1, S0358: 1, S0376: 1, S0444: 1, H0722: 1, S0278: 1, H0369: 1, H0431: 1, H0442: 1, H0613: 1, H0331: 1, H0574: 1, S0280: 1, L0021: 1, H0575: 1, H0421: 1, H0363: 1, H0184: 1, H0050: 1, H0373: 1, S0388: 1, S0250: 1, S0214: 1, H0252: 1, H0039: 1, H0124: 1, H0040: 1, H0494: 1, H0509: 1,		

							H0652: 1, S0144: 1, S0142: 1, S0210: 1, L0769: 1, L0637: 1, L0667: 1, L0648: 1, L0766: 1, L0775: 1, L0378: 1, L0542: 1, L0809: 1, L0543: 1, H0703: 1, H0726: 1, H0547: 1, H0519: 1, H0648: 1, S0380: 1, H0709: 1, S0136: 1, H0696: 1, S0406: 1, H0631: 1, L0740: 1, L0755: 1, L0731: 1, L0757: 1, L0758: 1, H0445: 1, H0595: 1, S0434: 1, L0361: 1, H0667: 1, S0276: 1 and S0462: 1.		
		1214441	191	102 - 377	378	Met-1 to Leu-6, Thr-32 to Glu-39.			
79	HBPOM70	1283382	89	374 - 1384	276	Tyr-41 to Thr-52, Gly-113 to Trp-120, Asn-143 to Lys-149, Glu-188 to Lys-210, Ser-222 to Leu-228, Glu-262 to Asp-267, Asp-299 to Asn-311.	L0777: 6, L0747: 4, L0731: 4, L0803: 3, L0749: 3, L0759: 3, S0474: 2, L0794: 2, L0744: 2, L0754: 2, L0750: 2, H0638: 1, H0208: 1, H0427: 1, S0250: 1, H0383: 1,		

							H0135: 1, H0488: 1, S0352: 1, L0638: 1, L0630: 1, L0804: 1, L0790: 1, L0792: 1, H0519: 1, H0710: 1, L0756: 1, L0752: 1 and H0445: 1.		
		1210399	192	373 - 1383	379	Tyr-41 to Thr-52, Gly-113 to Trp-120, Asn-143 to Lys-149, Glu-188 to Lys-210, Ser-222 to Leu-228, Glu-262 to Asp-267, Asp-299 to Asn-311.			
80	HMSMO35	1243922	90	407 - 727	277	Ser-100 to Lys-106.	S0426: 1		
		1212826	193	395 - 610	380				
81	HMUCI88	1256397	91	239 - 634	278	Thr-48 to Ser-54, His-62 to Arg-69, Gly-90 to Ala-100, Ser-120 to Ala-126.	S0222: 4, L0439: 4, L0747: 4, H0661: 3, L0803: 3, L0806: 3, L0752: 3, H0052: 2, H0620: 2, H0539: 2, H0686: 1, H0650: 1, S0212: 1, H0483: 1, S0418: 1, H0580: 1, S0007: 1, L0717: 1, S6022: 1, H0438: 1, H0592: 1, H0586: 1, H0635: 1, S0346: 1, H0581: 1, H0014: 1,		

							T0010: 1, H0266: 1, L0351: 1, H0494: 1, H0529: 1, L0769: 1, L0772: 1, L0764: 1, L0766: 1, L0774: 1, L0805: 1, L0659: 1, L0809: 1, L0647: 1, L0791: 1, L0793: 1, L0665: 1, H0144: 1, L0438: 1, L0352: 1, H0593: 1, H0689: 1, H0435: 1, H0522: 1, H0555: 1, L0741: 1, L0743: 1, L0744: 1, L0748: 1, L0751: 1, L0779: 1, L0755: 1, L0595: 1, S0424: 1 and H0677: 1.		
		1209766	194	1815 - 2042	381	His-49 to Cys-57.			
82	HMUDN51	1275158	92	54 - 299	279	Pro-46 to Ser-52, Ile-66 to Gly-74.	S0408: 4, L0774: 3, H0494: 2, H0529: 2, L0748: 2, S0354: 1, S0278: 1, T0040: 1, H0253: 1, H0012: 1, H0620: 1, H0594: 1, H0213: 1, H0181: 1, H0617: 1, S0036: 1, H0477: 1, H0102: 1, S0440: 1, L0645: 1,		

							L5574: 1, L0803: 1, L0518: 1, L0749: 1, L0752: 1 and H0445: 1.		
		1209998	195	45 - 290	382	Pro-46 to Ser-52, Ile-66 to Gly-74.			
83	HMAGC36	1262016	93	72 - 398	280	Pro-32 to Leu-39, Lys-56 to Cys-63, Arg-76 to Gly-88, Glu-99 to Gly-104.	S0278: 7, S0002: 6, H0521: 6, L0774: 5, S0144: 4, L0761: 4, L0777: 4, S0142: 3, L0803: 3, H0265: 2, H0556: 2, H0638: 2, S0426: 2, L0789: 2, L0741: 2, L0740: 2, S0420: 1, S0356: 1, S0444: 1, S0360: 1, L0717: 1, H0431: 1, H0333: 1, H0635: 1, H0618: 1, H0253: 1, H0505: 1, H0434: 1, H0078: 1, H0135: 1, H0100: 1, H0429: 1, H0494: 1, H0509: 1, L0640: 1, L0763: 1, L0770: 1, L0769: 1, L5575: 1, L0800: 1, L0768: 1, L0794: 1, L0499: 1, L0804: 1, L0806: 1, L0509: 1, L0807: 1, L0659: 1,		

							L0792: 1, L0663: 1, S0406: 1, L0751: 1, L0754: 1, L0747: 1, L0756: 1, L0779: 1, L0731: 1 and L0759: 1.		
		1219629	196	898 - 1251	383	Pro-32 to Leu-39, Lys-56 to Cys-63, Arg-76 to Gly-88, Glu-99 to Gly-104, Thr-107 to His-112.			
		1219632	197	2544 - 3047	384	Leu-60 to Glu-66, Gly-79 to Cys-86, Pro-99 to Pro-107, His-131 to Ser-140.			

Table 1C

Gene No.	Clone ID	Preferred Indication Identifier
1	HAGAN08	Immune/Hematopoetic, Neural/Sensory
2	HSANL54	Cancer
3	HSYHY70	Cancer
4	HEOUO75	Cancer
5	HSCPC08	Immune/Hematopoetic, Neural/Sensory, Reproductive
6	HSCPT22	Reproductive
7	HTLED86	Cancer
8	HTPKP89	Cancer
9	HSRFP52	Cancer
10	HDHEA83	Cancer
11	HFXBR92	Cardiovascular, Mixed Fetal, Neural/Sensory
12	HSYIH77	Cancer
13	HTAHS92	Immune/Hematopoetic
14	HAROV59	Connective/Epithelial
15	HDCCG73	Immune/Hematopoetic
16	HQAHD50	Cancer
17	HROBA16	Digestive
18	HTPJD12	Digestive, Excretory, Reproductive
19	HHAWD13	Cancer
20	HISFI83	Cancer
21	HISFV70	Cardiovascular, Digestive
22	HNSAB41	Cancer
23	HOCNY94	Digestive, Mixed Fetal, Reproductive
24	HAROG72	Cancer
25	HDACT07	Cancer
26	HLTIJ80	Immune/Hematopoetic
27	HNTZG72	Cancer
28	HNUCE33	Cancer
29	HODEM32	Reproductive
30	HPJHQ20	Reproductive
31	HQADO95	Endocrine
32	HTENS88	Cancer
33	HTLGC03	Cancer

34	HTLKQ55	Reproductive
35	HTOJF42	Immune/Hematopoetic
36	HTPHC19	Digestive, Immune/Hematopoetic
37	HDPHG50	Digestive, Immune/Hematopoetic, Neural/Sensory
38	HHEWS13	Immune/Hematopoetic
39	HOGCY01	Digestive, Immune/Hematopoetic, Reproductive
40	HPJGT38	Cancer
41	HTFMK11	Mixed Fetal, Neural/Sensory
42	HTSGQ95	Cancer
43	HLSAI43	Connective/Epithelial, Immune/Hematopoetic
44	HNBTF02	Cancer
45	HNSCC06	Cancer
46	HTENQ40	Reproductive
47	HCNCM78	Connective/Epithelial, Digestive, Reproductive
48	HCOKD57	Cancer
49	HRAEO74	Cancer
50	HTACM88	Cancer
51	HBWBI44	Neural/Sensory
52	HAGIF61	Cancer
53	HSYHD12	Cancer
54	HTAGF12	Immune/Hematopoetic, Neural/Sensory, Reproductive
55	HTHCA16	Cancer
56	HNFIQ15	Cancer
57	HNHPS28	Immune/Hematopoetic
58	HNTDN59	Cancer
59	HNTQM17	Immune/Hematopoetic, Reproductive
60	HNTTF76	Immune/Hematopoetic
61	HCFGD60	Digestive, Immune/Hematopoetic
62	HMUEP30	Cancer
63	HNSCA10	Cancer
64	HTPAO67	Cancer
65	HAZCB15	Reproductive
66	HSLFK66	Cancer

67	HCFPE46	Connective/Epithelial, Immune/Hematopoetic, Reproductive
68	HNGPB91	Immune/Hematopoetic
69	HRADV31	Cancer
70	HNBVG70	Cancer
71	HCFGK19	Immune/Hematopoetic
72	HNGOG04	Immune/Hematopoetic
73	HDCGC29	Immune/Hematopoetic
74	HNGNT27	Immune/Hematopoetic
75	HMUHD72	Cancer
76	HLYCK47	Cancer
77	HLYFJ90	Cancer
78	HMLHD54	Cancer
79	HBPOM70	Cancer
80	HMSMO35	Immune/Hematopoetic
81	HMUCI88	Cancer
82	HMUDN51	Cancer
83	HMAGC36	Cancer

Table 2

Clone ID NO:Z	Contig ID:	SEQ ID NO:X	Analysis Method	PFam/NR Description	PFam/NR Accession Number	Score/ Percent Identity	NT From	NT To
HAGAN08	1212501	11	blastx.2	PRO1847.	sp|Q9P191|Q9P191	53% 76%	1015 1065	920 1015
HSANL54	1262040	12	blastx.2	Y24F12A.1 PROTEIN.	sp|Q9U2Q7|Q9U2Q7	38% 35%	829 679	1479 909
HSANL54	1191032	95	HMMER 2.1.1	PFAM: Uncharacterized protein family	PF01026	291.1	274	-271
			blastx.14	similar to E.coli hypothetical 29.6 KD protein(P1:YIGW_ECOLI) [Homo sapiens]	gi|1504018|dbj|BAA1 3208.1|	99%	8	562
HSYHY70	1268180	13	blastx.2	SERINE HYDROXYMETHYLTR ANSFERASE, MITOCHONDRIAL PRECURSOR 1 1	sp|P34897|GLYM_H UMAN	99%	100	1581
HSYHY70	1225974	96	blastx.2	SERINE HYDROXYMETHYLTR ANSFERASE, MITOCHONDRIAL PRECURSOR 1 1	sp|P34897|GLYM_H UMAN	98%	87	635
HEOUO75	1283143	14	WUblastx	(AF166382) serpentine	gb|AAF00617.1|AF1	43%	1413	1688

			.64	receptor [Mus musculus]	66382_1	29%	1651	2373
HSCPC08	1262036	15	blastx.2	conserved hypothetical protein VCA0703 [imported] - Vibrio cholerae (group O1 strain N16961)	pir|D82426|D82426	33%	38	553
HSCPC08	1213061	98	blastx.2	conserved hypothetical protein VCA0703 [imported] - Vibrio cholerae (group O1 strain N16961)	pir|D82426|D82426	31%	18	533
HSCPT22	1243895	16	WUblastx .64	arginine-rich protein [Homo sapiens]	gb|AAB08753.1|	63%	185	652
HSCPT22	1209266	99	blastx.2	arginine-rich protein - human	pir|S27956|S27956	63%	174	641
HTLED86	1253125	17	blastx.2	PUTATIVE SEVEN PASS TRANSMEMBRANE PROTEIN.	sp|O60478|O60478	53%	7	753
HTLED86	1222077	100	blastx.2	PUTATIVE SEVEN PASS TRANSMEMBRANE PROTEIN.	sp|Q9JHD9|Q9JHD9	55%	527	1330
HTLED86	1221659	101	blastx.14	Putative seven pass transmembrane protein.	sp|AAF73259|AAF73 259	59% 81%	166 1	522 33
HTPKP89	1263310	18	WUblastx .64	(AK027056) unnamed protein product [Homo sapiens]	dbj|BAB15641.1|	96% 98%	205 524	549 1117

HTPKP89	1213121	102	blastx.2	CDNA: FLJ23403 fis, clone HEP18857.	sp|BAB15641|BAB15641	98%	196	681
HSRFP52	1254537	19	blastx.2	STRABISMUS.	sp|O45030|O45030	51% 37%	123 63	1280 332
HSRFP52	745408	103	blastx.2	STRABISMUS.	sp|O45030|O45030	48% 34% 31%	479 58 58	1276 468 327
HSRFP52	1182209	104	blastx.14	(AF044208) Strabismus [Drosophila melanogaster]	gi|2854044|gb|AAC02533.1|	52% 36% 68% 38%	525 354 192 267	956 536 266 344
HDHEA83	1217946	106	HMMER 2.1.1	PFAM: Transmembrane 4 family	PF00335	75.7	220	585
HFXBR92	1243870	21	blastx.2	PRO1722.	sp|Q9P195|Q9P195	66%	270	560
HFXBR92	1208739	108	blastx.2	PRO1722.	sp|Q9P195|Q9P195	66%	258	548
HSYIH77	1276392	22	HMMER 2.1.1	PFAM: TPR Domain	PF00515	69.2	926	1009
			blastx.2	Hypothetical 57.4 kDa protein.	sp|BAB12304|BAB12304	100% 25% 26%	1043 839 770	2548 1003 883
HTAHS92	1243918	23	blastx.2	CDNA FLJ20378 FIS, CLONE KAIA0536.	sp|Q9NX85|Q9NX85	57% 46%	618 1428	328 1384
HTAHS92	1213187	111	blastx.2	PRO2550.	sp|AAG35515|AAG35515	72% 69% 66%	587 649 743	459 581 672
HAROV59	1272018	24	blastx.2	triacylglycerol lipase (EC 3.1.1.3) precursor, gastric - human	pir|S07145|S07145	58% 43% 46%	52 489 846	489 884 1085

HAROV59	1209631	113	HMMER 2.1.1	PFAM: alpha/beta hydrolase fold	PF00561	31.2	372	590
			blastx.2	lysosomal acid lipase (EC 3.1.1.-) / sterol esterase (EC 1	pir|S41408|S41408	68% 81%	120 593	590 640
HDCCG73	1243884	25	blastx.2	UNNAMED PORTEIN PRODUCT.	sp|Q9N083|Q9N083	56% 64%	520 305	296 222
HDCCG73	1209263	114	blastx.2	UNNAMED PORTEIN PRODUCT.	sp|Q9N083|Q9N083	56% 64%	575 360	351 277
HROBA16	1243878	27	blastx.2	Hypothetical 12.9 kDa protein.	sp|BAB12124|BAB12124	48% 56%	926 1132	1162 1239
HTPJD12	1262048	28	WUblastx.64	(AX058634) unnamed protein product [Homo sapiens]	emb|CAC22532.1|	92% 83%	8 386	448 694
HTPJD12	1209268	118	blastx.2	(AX058634) unnamed protein product [Homo sapiens]	emb|CAC22532.1|	92% 83%	3 384	446 692
HHAWD13	1272864	29	HMMER 2.1.1	PFAM: Ank repeat	PF00023	202.9	1203	1301
			blastx.2	hypothetical protein DKFZp434D2328.1 - human (fragment)	pir|T42691|T42691	60% 29% 29% 28% 30% 30% 27% 28% 33%	24 30 24 15 30 63 15 12 411	1634 1622 1580 1577 1580 1307 1577 1586 1580

						30% 28% 28% 47% 43%	153 363 504 1591 1603	1580 1610 1610 1725 1725
HHAWD13	1209632	119	HMMER 2.1.1	PFAM: Ank repeat	PF00023	62	382	480
			blastx.2	hypothetical protein DKFZp434D2328.1 - human (fragment)	pir|T42691|T42691	75% 31% 30% 30% 31% 28% 39% 30% 32% 28% 36% 41%	1 37 28 13 73 10 310 7 22 127 337 385	627 612 555 618 636 606 609 600 612 609 636 615
HNSAB41	1268184	32	HMMER 2.1.1	PFAM: Zinc finger, C3HC4 type (RING finger)	PF00097	36.3	1049	1171
			WUblastx .64	(AK018582) putative [Mus musculus]	dbj|BAB31291.1|	92%	221	1504
HNSAB41	1212804	122	blastx.2	BRAIN CDNA, CLONE MNCB-3816, SIMILAR TO AF171875 G1-RELATED 1	sp|Q9JJF8|Q9JJF8	77% 94%	206 861	1015 1490

HAROG72	1281478	34	blastx.2	NEURONAL THREAD PROTEIN AD7C-NTP.	sp|O60448|O60448	65% 67% 61% 66% 66% 70% 52% 49% 58% 35% 47% 73% 44% 52% 57% 51% 37% 40% 45% 40% 34%	230 2040 227 2046 199 2006 846 858 847 214 817 106 2040 1958 1950 750 874 2020 816 237 218	30 1867 36 1885 29 1884 670 670 731 35 689 38 1939 1884 1894 670 668 1943 721 163 114
HAROG72	1209767	124	blastx.2	CDNA FLJ20489 FIS, CLONE KAT08285.	sp|Q9NX17|Q9NX17	71% 46%	202 390	14 310
HDACT07	1280454	35	blastx.2	CDNA FLJ12761 fis, clone NT2RP2001378, weakly similar to 1	sp|BAB14261|BAB14261	100%	12	1244
HDACT07	1209253	125	blastx.2	CDNA FLJ12761 fis, clone NT2RP2001378, weakly similar to 1	sp|BAB14261|BAB14261	80% 85% 88%	2 956 303	706 1156 410

						25%	309	461
HNTZG72	1246154	37	HMMER 2.1.1	PFAM: Monocarboxylate transporter	PF01587	30.9	104	373
			blastx.2	CDNA: FLJ21463 fis, clone COL04765.	sp|BAB15071|BAB1 5071	66%	722	1060
HNTZG72	1209378	127	HMMER 2.1.1	PFAM: Monocarboxylate transporter	PF01587	30.9	85	354
			blastx.2	BRAIN CDNA, CLONE MNCB-2717.	sp|Q9JJC0|Q9JJC0	36%	1	276
HNUCE33	1275160	38	blastx.2	Hypothetical 3.2 kDa protein.	sp|AAG10068|AAG1 0068	100%	983	891
HNUCE33	1209149	128	blastx.2	(AL121581) dJ1022E24.4 (novel protein) [Homo sapiens]	emb|CAC17006.1|	48%	216	878
HODEM32	1253127	39	blastx.2	CDNA: FLJ21463 fis, clone COL04765.	sp|BAB15071|BAB1 5071	69%	1868	1581
HQADO95	1276422	41	blastx.2	CDNA FLJ20489 FIS, CLONE KAT08285.	sp|Q9NX17|Q9NX17	68%	1079	807
HTENS88	1243927	42	blastx.2	CG7530 PROTEIN.	sp|Q9VFG7|Q9VFG7	34% 32%	18 689	428 832
HTENS88	1213009	132	blastx.2	CG7530 PROTEIN.	sp|Q9VFG7|Q9VFG7	34%	11	421
HTLGC03	1261928	43	blastx.2	DJ1184F4.4 (NOVEL PROTEIN SIMILAR TO NUCLEOLAR PROTEIN 4 1	sp|Q9NQF5|Q9NQF5	99% 100% 27%	923 843 1385	1375 926 1471
HTLGC03	1227183	135	blastx.14	probable importin beta-4 subunit - fission yeast (Schizosaccharomyces	pir|T39449|T39449	24% 36% 30%	874 2080 2320	401 1886 2156

				pombe)		30% 33% 29% 20% 28% 32% 33% 33% 27% 53% 28% 24% 34%	1501 1768 1483 2314 1426 2026 2507 829 1483 1861 1786 1219 1171	1298 1634 1319 2171 1343 1916 2445 749 1376 1823 1703 1133 1094
HTLKQ55	1243896	44	blastx.2	CDNA FLJ20160 FIS, CLONE COL09072.	sp|Q9NXM3|Q9NX M3	26% 38%	474 1050	977 1151
HTOJF42	1261944	45	blastx.2	PRO2550.	sp|AAG35515|AAG3 5515	66% 80%	407 657	655 719
HDPHG50	1268191	47	blastx.2	HYPOTHETICAL 18.9 KDA PROTEIN (FRAGMENT).	sp|Q9Z0T1|Q9Z0T1	98%	597	1097
HDPHG50	1213570	139	HMMER 2.1.1	PFAM: Protein phosphatase 2C	PF00481	119.3	460	945
			blastx.2	HYPOTHETICAL 18.9 KDA PROTEIN (FRAGMENT).	sp|Q9Z0T1|Q9Z0T1	97%	586	948
HPJGT38	1209290	50	blastx.2	CDNA FLJ20378 FIS, CLONE KAIA0536.	sp|Q9NX85|Q9NX85	56% 73%	87 347	344 403
HTFMK11	1276752	51	blastx.2	CDNA: FLJ21463 fis,	sp|BAB15071|BAB1	70%	486	749

				clone COL04765.	5071	65%	728	787
HTFMK11	1212928	142	blastx.2	CDNA FLJ12155 fis, clone MAMMA1000472.	sp|BAB13989|BAB13989	77%	541	702
HTSGQ95	1280458	52	blastx.2	TNF-a-inducible RNA binding protein.	sp|AAG15396|AAG15396	100% 98%	2357 1335	2722 1631
HTSGQ95	1213625	144	blastx.2	CDNA FLJ20489 FIS, CLONE KAT08285.	sp|Q9NX17|Q9NX17	67%	10	291
HLSAI43	1243888	53	blastx.2	CDNA FLJ20489 FIS, CLONE KAT08285.	sp|Q9NX17|Q9NX17	59% 87% 81%	763 764 489	512 741 457
HLSAI43	1213409	146	blastx.2	UNNAMED PROTEIN PRODUCT.	sp|Q9N032|Q9N032	61% 61% 85%	595 480 494	494 442 474
HNBTF02	1253163	54	WUblastx .64	(AK024780) unnamed protein product [Homo sapiens]	dbj|BAB15000.1|	98% 100% 89%	604 251 1330	1230 601 1791
HNBTF02	1226356	147	blastx.2	CDNA: FLJ21127 fis, clone CAS06212.	sp|BAB15000|BAB15000	98% 89%	373 1453	1353 1914
HNSCC06	1263307	55	WUblastx .64	(AK022749) unnamed protein product [Homo sapiens]	dbj|BAB14223.1|	100% 99%	106 533	540 1618
HNSCC06	1209025	148	blastx.2	CDNA FLJ12687 fis, clone NT2RM4002532, weakly similar to 1	sp|BAB14223|BAB14223	98% 70% 66%	89 894 973	892 1046 1008
HTENQ40	1243926	56	HMMER 2.1.1	PFAM: 7 transmembrane receptor (rhodopsin family)	PF00001	67	204	458
			blastx.2	(AF247656) odorant	gb|AAG09780.1|AF2	51%	84	554

				receptor M72 [Mus musculus]	47656_1	51%	520	999
HTENQ40	1213048	149	HMMER 2.1.1	PFAM: 7 transmembrane receptor (rhodopsin family)	PF00001	67	197	451
			blastx.2	OLFACTORY RECEPTOR 2 (FRAGMENT).	sp|Q90806|Q90806	45%	65	637
HCOKD57	1271607	58	blastx.2	(AF299340) CD164 isoform delta 4 [Homo sapiens]	gb|AAG53905.1|	70%	64	621
HCOKD57	1213043	152	blastx.2	(AF299340) CD164 isoform delta 4 [Homo sapiens]	gb|AAG53905.1|	48%	243	572
HRAEO74	1209635	59	blastx.2	MIB002 PROTEIN.	sp|Q9NQ90|Q9NQ90	36% 42%	425 288	1228 329
HTACM88	1253076	60	blastx.2	UROKINASE-TYPE PLASMINOGEN ACTIVATOR RECEPTOR.	sp|Q12876|Q12876	100%	1409	1807
HTACM88	1213431	153	blastx.2	NEURONAL THREAD PROTEIN AD7C-NTP.	sp|O60448|O60448	70% 67% 60% 38% 42% 52%	126 138 10 4 9 13	257 257 78 81 71 69
HBWBI44	1159379	155	blastx.2	PRO1902 PROTEIN.	sp|Q9UHT1|Q9UHT1	72% 67%	118 246	249 338

HSYHD12	1280343	63	HMMER 2.1.1	PFAM: Filamin/ABP280 repeat.	PF00630	31.5	376	603
			WUblastx .64	(BC001297) Unknown (protein for MGC:5302) [Homo sapiens]	gb|AAH01297.1|AAH01297	100%	301	1683
HSYHD12	1209769	157	HMMER 2.1.1	PFAM: Filamin/ABP280 repeat.	PF00630	31.5	387	614
			blastx.2	ER PROTEIN 58.	sp|Q9JHP7|Q9JHP7	89% 94%	312 1364	1379 1816
HTAGF12	1276746	64	blastx.2	CDNA: FLJ21463 fis, clone COL04765.	sp|BAB15071|BAB15071	56% 60%	2467 2628	2297 2464
HTHCA16	1243880	65	WUblastx .64	(BC001129) Unknown (protein for MGC:2463) [Homo sapiens]	gb|AAH01129.1|AAH01129	90%	17	994
HNHPS28	1243890	67	WUblastx .64	(AF130051) PRO0898 [Homo sapiens]	gb|AAG35479.1|AF130117_10	81% 66%	837 1069	805 833
HNTDN59	1280527	68	WUblastx .64	(AL136581) hypothetical protein [Homo sapiens]	emb|CAB66516.1|	100%	1611	2447
HNTDN59	1215793	165	blastx.2	CDNA FLJ12799 fis, clone NT2RP2002078, weakly similar to 1	sp|BAB14277|BAB14277	100%	1682	2437
HNTDN59	1210379	167	HMMER 2.1.1	PFAM: Enoyl-CoA hydratase/isomerase family	PF00378	330.6	-73	-573
HNTQM17	1283173	69	WUblastx .64	(AF153906) erythroid membrane-associated protein ERMAP [Mus musculus]	gb|AAF31162.1|AF153906_1	56% 27% 32% 80%	245 536 3370 787	682 829 3453 1668

HNTQM17	1209252	168	blastx.2	ERYTHROID MEMBRANE-ASSOCIATED PROTEIN ERMAP.	sp|Q9JLN5|Q9JLN5	55% 32%	235 11	594 76
HNTTF76	1243907	70	blastx.2	CDNA: FLJ21394 fis, clone COL03536.	sp|BAB15056|BAB15056	65% 55%	1053 1109	847 1056
HMUEP30	1262057	72	blastx.2	54TMP.	sp|O95070|O95070	57%	100	942
HMUEP30	1209865	171	blastx.2	54TMP.	sp|O95070|O95070	58%	90	518
HNSCA10	1268201	73	HMMER 2.1.1	PFAM: GNS1/SUR4 family	PF01151	191.8	279	923
			WUblastx .64	(AK027031) unnamed protein product [Homo sapiens]	dbj|BAB15632.1|	100%	129	923
HNSCA10	1209403	172	HMMER 2.1.1	PFAM: GNS1/SUR4 family	PF01151	132.7	266	652
			blastx.2	CDNA: FLJ23378 fis, clone HEP16248.	sp|BAB15632|BAB15632	97%	116	652
HTPAO67	1280558	74	blastx.2	DJ737E23.1 (EGF-LIKE DOMAINS CONTAINING C1Q/MBL/SPA RECEPTOR 1	sp|Q9NPY3|Q9NPY3	100%	3	401
HAZCB15	1243853	75	blastx.2	PRO2550.	sp|AAG35515|AAG35515	74%	59	379
HAZCB15	1209801	175	blastx.2	PRO2550.	sp|AAG35515|AAG35515	76%	58	354
HSLFK66	1271609	76	blastx.2	ybhR protein - Escherichia coli	pir|H64815|H64815	100% 29%	597 2	1700 478

HSLFK66	1224406	176	blastx.2	ABC-type transport protein ybhF - Escherichia coli	pir|B64816|B64816	99%	151	1899
HCFPE46	1243901	77	blastx.2	(AF275266) PDRP [Rattus norvegicus]	gb|AAG50204.1|	82% 70% 61%	425 227 65	559 328 169
HCFPE46	1223989	177	blastx.2	(AF275266) PDRP [Rattus norvegicus]	gb|AAG50204.1|	57% 59%	414 66	548 158
HNGPB91	1253113	78	blastx.2	CDNA: FLJ21463 fis, clone COL04765.	sp|BAB15071|BAB15071	48% 66%	5 1797	229 1480
HNGPB91	1212875	178	blastx.2	CDNA: FLJ21394 fis. clone COL03536.	sp|BAB15056|BAB15056	46%	4	222
HRADV31	1275159	79	blastx.2	hypothetical protein DKFZp434G145.1 - human (fragment)	pir|T17335|T17335	99%	1471	2019
HCFGK19	1253156	81	blastx.2	CDNA: FLJ21463 fis, clone COL04765.	sp|BAB15071|BAB15071	78%	1675	1391
HNGNT27	1261927	84	blastx.2	NEURONAL THREAD PROTEIN AD7C-NTP.	sp|O60448|O60448	65% 52% 52% 49% 44% 41% 51% 50% 41%	1711 1732 1087 1087 1710 999 1677 1648 1710	1556 1538 911 899 1516 829 1555 1547 1558
HMUHD72	1281806	85	blastx.2	conserved hypothetical protein NMB0419	pir|F81200|F81200	33% 35%	854 827	1225 1228

				[imported] - Neisseria meningitidis (group B strain MD58)				
HMUHD72	1209710	187	blastx.2	hypothetical protein [imported] - Vogesella indigofera	pir|T46587|T46587	28% 26%	773 890	1360 1414
HLYCK47	1272921	86	HMMER 2.1.1	PFAM: C1q domain	PF00386	247.7	387	752
			blastx.2	complement subcomponent C1q chain C precursor - human	pir|S14351|C1HUQC	93%	72	761
HLYCK47	1221159	188	HMMER 2.1.1	PFAM: Collagen triple helix repeat (20 copies)	PF01391	42	227	406
			blastx.2	complement subcomponent C1q chain C precursor - human	pir|S14351|C1HUQC	66% 53%	129 119	830 358
HLYCK47	1221167	189	HMMER 2.1.1	PFAM: C1q domain	PF00386	247.7	468	833
			blastx.2	complement subcomponent C1q chain C precursor - human	pir|S14351|C1HUQC	100% 53% 30% 25% 52% 52% 34% 36%	444 108 118 118 198 198 208 175	842 347 411 399 254 263 330 249
HMLHD54	1243834	88	HMMER 2.1.1	PFAM: Alpha-L-fucosidase	PF01120	77	111	314

			blastx.2	DJ20N2.5 (NOVEL PROTEIN SIMILAR TO FUCOSIDASE, ALPHA-L-1, 1	sp|Q9UJM5|Q9UJM5	99% 98%	298 75	1287 305
HMLHD54	1214441	191	HMMER 2.1.1	PFAM: Alpha-L-fucosidase	PF01120	77	138	341
			blastx.2	DJ20N2.5 (NOVEL PROTEIN SIMILAR TO FUCOSIDASE, ALPHA-L-1, 1	sp|Q9UJM5|Q9UJM5	98% 98% 100%	325 183 620	615 332 703
HBPOM70	1283382	89	HMMER 2.1.1	PFAM: Sodium/hydrogen exchanger family	PF00999	223.1	374	919
			blastx.2	SODIUM/HYDROGEN EXCHANGER 6 (NA(+)/H(+) EXCHANGER 6) 1	sp|Q92581|NAH6_HUMAN	63%	20	1360
HBPOM70	1210399	192	HMMER 2.1.1	PFAM: Sodium/hydrogen exchanger family	PF00999	223.1	373	918
			blastx.2	SODIUM/HYDROGEN EXCHANGER 6 (NA(+)/H(+) EXCHANGER 6) 1	sp|Q92581|NAH6_HUMAN	61%	34	1218
HMSMO35	1243922	90	blastx.2	NEURONAL THREAD PROTEIN AD7C-NTP.	sp|O60448|O60448	63% 63% 60% 54% 51% 38%	1209 1181 1172 514 520 1065	1481 1420 1366 723 705 1409

						54% 43% 34% 42% 45% 46% 38% 52% 47% 58% 39% 39% 48%	530 581 584 1293 621 645 577 520 1353 1181 1351 729 705	667 814 799 1409 779 779 753 588 1478 1267 1458 797 779
HMUDN51	1275158	92	blastx.2	CDNA FLJ13875 fis, clone THYRO1001374, weakly similar to 1	sp|BAB14734|BAB1 4734	99%	218	1117
HMUDN51	1209998	195	blastx.2	CDNA FLJ13875 fis, clone THYRO1001374, weakly similar to 1	sp|BAB14734|BAB1 4734	98%	209	490
HMAGC36	1219632	197	blastx.14	hypothetical protein F16H11.1 - Caenorhabditis elegans	pir|T16084|T16084	53% 41% 57% 36% 36% 32% 46%	212 761 1103 8 584 1133 662	526 949 1243 202 682 1243 706

TABLE 3				
Gene No.	cDNA Clone ID	NT SEQ ID NO: X	Contig ID	Public Accession Numbers
1	HAGAN08	11	1212501	Z69655
2	HSANL54	12	1262040	BF476265, AI797047, AU130755, BE048483, BE697125, AI738659, AW500849, AL533682, BF894584, BF956040, BF360667, AW375079, BF752028, AW378658, BE831601, AA502615, BF895374, BE006128, AW504330, BF761857, BF982636, D86972, and AC008116.
2	HSANL54	94	1213405	AI738659, AI627779, AW083624, AW204211, AA054944, AW204545, AI742189, AW007439, AW518027, BF894584, AI092337, AW274827, AI830887, AA776446, AI827903, BF478230, AW589942, AI936767, AI766902, AW245965, BF732759, AI499238, BE502033, AI871105, AU152652, AI968436, BE348742, BF216850, AI580690, BE673999, AA778810, AI022038, BE326496, AW339794, BE327376, T32765, AI373613, BE856484, AA894920, AA677783, BG150571, Z19484, AA019610, T03681, AA523505, H98846, H99004, AI634772, BE467301, AW167571, N59382, N24858, AI796457, BF433527, BF244404, AI783639, AI274439, R69539, Z39827, BF218582, BF216244, BF215884, BF185903, BF752028, AI202218, AW375079, BF217306, BF217602, R90822, BF901088, H09277, BF245839, AI655908, AI474534, BE697125, H27493, R01271, AI202208, BF215441, T97706, R90809, F01772, H15567, BE831601, BF082752, BE092521, BG170453, AA627824, BF895374, AW843847, BE006128, BF956040, AI760935, T31294, BF218863, BE092006, AW504330, BE092011, BF218445, D86972, and AC008116.
2	HSANL54	95	1191032	BF476265, AI797047, AU130755, BE048483, AW500849, AL533682, AW378658, BF360667, BE697125, AA502615, BF761857, BF982636, AC008116, and D86972.
3	HSYHY70	13	1268180	AL515677, AL517191, AL517711, AL514438, AL514588, AL517885, AL519061, AL515998, AL519098, AL516935, AL515676, AL517120, AL517190, AL517884, AL517710, AL519060, BE738403, BE561838, BE798895, AU118358, BF307302, BG257246, BE250748, AW411251, BE300412, BE250263, BF343263, BE300033, BE250390, BE795083, BF303631, BF309556, AU125632, AL516936, BE797752, AL515997, AW411250, BG034145, AL517121, BE299994, BE560803, BE300378, AU142313, BE792083, BG255993, BG055192, BE299989, BF203939, AU124938, BE785439, BE250578, BF310044, BE250397, BE562180, BE300321, AI653986,

				AI638143, BE797897, BF307049, BE299885, BF037599, BE735822, BE799541, BE300481, BE297154, BE513833, BF310125, BE780981, BF204514, BE561576, BE293953, AU130353, BE300435, BF304097, BE299626, BE786047, AW411277, BF309568, BF305349, BE798279, AU143226, AU117330, AU143785, BF305596, BE902829, BE299921, BE273916, AV707635, BF528416, BE298040, AL135023, AW410516, BF308940, BE675245, AU125188, AI609108, BF308856, BE250291, BF307501, AU125219, BE300090, BE900387, BE792628, BE798367, AL515142, BE250640, BF310726, AW410724, BE294991, BE891362, AW411276, AW411540, BE439939, BF307530, AW410822, BF308240, BE731826, AU132298, BF305676, BE257914, BE897171, BE298518, BF795096, BE396043, BE252605, BE278737, BE731843, AW411012, BF304483, BE787933, BE300122, BE385206, BF310041, BF306036, BE786905, AW411541, BE791288, BE790276, AW410899, AI591086, BE795734, BF307367, BE797954, AI951452, BE298091, BF203813, AW411176, BE740411, BF304937, BE297914, BE799403, BE261174, AI421521, BE299946, BF795637, BE295043, AW411490, AU126059, AU125191, AU128674, BF305858, BE250322, BF303832, BG105971, BF307028, BF308569, AW249463, BE293980, BE741670, BE299152, AW410455, BE797591, BE544882, BE297823, BF310023, AI691054, BE673335, BE903787, BE296989, BE793976, AW474021, AU122609, BE297349, BF796273, AW410898, BF304526, BE295105, BE799645, BF309859, BF308782, BE297671, BF526018, AU134144, BE250671, BE294777, BF305577, BE293999, BE544505, BF204057, BF204274, BF309146, AI700140, BE298644, BG236298, BF304457, BF307427, BF308404, BE294532, BE622198, BE297295, AU142593, BF303687, BF981474, BE869331, BF205556, BE019318, AI950991, BF313634, AW410459, BE297999, AU142292, BE294766, AW249523, BE269794, BE298714, BE299087, BE300314, BE379055, AI632983, BE296223, AW410456, AW411486, BG257264, BE266415, BF206062, BE294403, BE267620, AW411175, AI887587, AW273145, BE298448, BF981469, BF206061, BE740956, BF311467, BE257079, BF204911, BE744199, AI817987, BF204997, L11932, X91902, U23143, Z62251, and Y12331.
3	HSYHY70	96	1225974	BE250263, BE250578, BF308856, BE297823, BF203915, BF304457, BF305858, BF304526, BE297349, BE298518, BE298644, BE295105, BF309183, BF307427, BF310125, BE294298, BF204274, BF306271, BE297999, BF310023, BE298714, BF303687, BE792083, BE741670, AL515677, BF795096, BE296989, AL515998,

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4	HEOUO75	14	1283143	BF183209, BE672513, AW962455, AW468228, AA593830, BE831720, AW339591, AW440986, BE241639, AA367270, AW440877, AW592568, AI807052, and AF111851.
4	HEOUO75	97	1228107	and BE241639.
5	HSCPC08	15	1262036	AW027686, AI333632, AI828510, AA699811, AI056812, AI571877, AI684189, AI684527, AI033940, AI090421, AI752451, AA953377, AL157674, BF970990, BF055737, AL042628, AL042382, AI857296, AI282655, AI433976, AI866457, AI340582, AL119457, AI591316, AI570384, AI287326, AI289937, AW190042, AI933589, AL039086, AW105601, AI702406, AI610756, AI439478, AW071417, AI829327, AI468872, AL119863, AI500077, AW169634, AW084219, AI274541, AI475817, BF339322, AI280747, AI572787, AW075351, BG030364, AW827228, AI859511, AI571909, AI569583, BF527014, AI610645, AI800453, AI800433, AA427700, BE964621, AL135661, BF817926, BE895585, AW167410, AI590118, AW162071, AL044207, BG113385, AI801152, AA225339, AI668893, BG058398, AI815855, BG164558, AI524671, BE781369, AI680498, AW827276, AI632408, BG249582, AL038445, AI312428, BE785868, AV746964, BE047737, AW150578, AW303152, BF701153, BE048071, AW301409, AW002342, AI923768, AV760102, BF970449, AW103371, AI250663, BG110684, AI587143, AW132056, BG027280, AI619817, AI343059, AI813579, AL120854, AI609592, AW074993, BG164371, AI744923, AI349933, AI349614, BE910703, AV682229, BG168185, BF342070, AI439745, AW827206, BG168549, BF811780, BE047952, AI348897, AI349004, AV738991, AI282326, AI362637, AI475430, AI274508, AI564247, AI282281, AI539808, AA508692, AI312152, AI270707, BF885675, AW075084, AW148320, AW268220, AI349937, BG168696, AV757639, AV708075, AV755311, AW129916, AW301505, AI439717, AI307708, AI922901, AI336513, BF726348, AI281773, AV682567, AL036802, BG026428, AI348895, AW269097, AI648684, AV681759, AW827289, AI431424, AI608936, AI307520, BG023758, BF341801, BE910373, BE876038, AI306613, AI872711, AW268253, AI696612, AI567612, AI433384, BG180034, AW169653, BF968205, AL036396, AI620284, BG024332, AW827203, AI349645, AW302992, AI874166, BG179633, AI537677, BF882343, AI874109, N42321, AI811353, AI500659, BE139128, AL120736, AW023590, AW302988, AI624604, AI345735, BF904244, AI612885, BG113299, AI784252, AI818206, BF792469, AI634224, BG163618, AW059837, AI475394, BG260037, AL036980, AI554245, AI597750, AI621209, AI702433, AW149227,

				AI497733, AW999049, AV757865, AI571133, AI886753, BF793244, BG257535, BG165051, BG112879, BF814335, AL134830, BE894455, AI783504, BF924882, AI869367, BF971016, AI648663, BF726198, BG110517, BF812933, AL036403, AW072930, AL120853, AW238730, BF792961, AI590120, BF038131, BG180996, AI889133, AL040243, BE964876, AA572758, BE965192, AI499285, BG114104, AI269862, BG179993, BE909398, BE018711, AI636445, AI612759, AL045266, AK024538, I48979, I48978, Y11587, A08916, AL117583, AF090896, AL050277, AK000652, I89947, AL359596, AF078844, AL117585, A08913, U42766, A08910, AF119899, AF130075, AL133016, I89931, AK026592, AR087170, AK026741, AB048954, AK026647, AL050393, AF116602, AK000618, AL049452, AB047904, AF113677, AK026959, AF061943, AL137557, AL110221, AL137271, AL133557, AK025772, U00763, AB052191, Y16645, AL049430, AF113013, AF116631, AK025491, AF111847, S68736, AB051158, AF090943, AK025967, AF218014, AL133075, AB049758, L31396, AL050108, AK026542, L31397, AF113690, AF116639, AL110196, AB052200, AL442082, AF146568, AF079765, AK024524, AF091084, AR011880, AF017437, AB048953, AF111851, A08909, AL137538, AK027164, AF158248, X63574, AK025958, AL390167, AF116649, AK025524, AF113676, AB019565, AL049464, AK000445, AL133080, AF113691, AF207829, AK026532, AK000718, AX006092, AF116644, AL137550, AK027096, AF130066, AK026583, AF242189, AF104032, AL080124, AL359615, AL110225, AF314091, AX019230, AF113019, AL162083, X82434, A93016, AL133640, AL049314, AF130105, AJ238278, AF017152, AL359601, E07108, AL050116, AL122093, AF118094, AB048964, Y11254, AL137459, AL117460, AR079032, AF125948, AX026824, AX026823, A58524, A58523, AF118064, AX046603, AF118070, AL122050, S78214, AF113699, AF130059, AJ242859, AR059958, AL133560, AL050146, AL442072, AL157431, AL133093, AF119875, AL359618, AF119878, AB047615, AK000137, AF177336, AF116682, AK025084, X84990, AF116646, AK026927, AF090901, AF130104, AL050138, AL133606, AX019229, AF113694, AL122123, AK027113, Z82022, AF090934, AK000647, AK026045, AF119871, E02349, AF183393, AK025092, AL117457, AL050149, AF177401, AL080137, AL137527, AL133565, AF106862, AF116691, AL359941, AF116688, E03348, AF113689, A65341, AJ000937, AL049382, AF130092, AK026865, AL080060, AL389982, X96540, AK026855, AK026353,

				AB041801, AF219137, AF090900, AF090903, AF125949, AL117394, AL122121, AL389978, AK026744, AF119909, AF225424, AK026784, AL162006, AF130099, AK026452, AL117435, I03321, AL050024, AK026534, AL049466, AF130110, AF097996, X70685, AK026608, AF130082, AL137463, AL353940, AK026526, AK026504, A77033, A77035, AK025339, AK025414, AK000083, AK027204, AF138861, AK000323, AK026629, AK026086, AK000432, AK026947, AL122098, U91329, AK000614, X72889, E07361, AF260566, AL049938, AL080127, AL096744, AL137648, AF130077, A03736, AL133113, AK027116, AK025391, AK025906, U80742, U35846, AK026533, AL359583, and AF116654.
5	HSCPC08	98	1213061	AW027686, AI333632, AI828510, AA699811, AI571877, AI056812, AI684189, AI684527, AI033940, AI090421, AI752451, AA953377, and AL157674.
6	HSCPT22	16	1243895	AI807908, AI214900, AV657190, AA018863, F31353, AA885943, AA725810, AI349772, AA018896, BE048071, AI687376, BE047863, AL047042, BE785905, BF343172, AV655645, AI433976, BF968493, AW071349, BE048163, BG179993, AL515041, AI868831, AL121270, AL513907, AI608667, AI436456, AI567351, AW827203, BG036846, BG058208, AL135661, BE964700, AW117882, AI433157, AI690751, AI349645, AI500077, BG179633, AI702406, BF724691, AL513911, AW268253, BF883916, AI064830, BG260037, BG168696, AW303152, BF795712, AI815383, AL513597, BF971016, AV712838, AL513553, AL036146, BE964812, BF793644, BE048026, BF054789, AV682249, AL047763, AL036396, AL046849, AL045500, BG252929, BE048179, BF726421, AL513803, BE877769, AI687728, BG108147, AI679724, AL514919, BF813978, AV711509, AL119049, BE965556, BF727212, BF792099, AI538716, BF970731, BE964633, AL119791, BE543089, AI568870, AV682266, AV755613, AW827211, BF812933, BG250190, BE018711, AI349004, AW162071, AW999049, AV682809, AV717179, AL036802, AL121365, AL514627, AI349933, AI499393, AW089572, AI873731, AI500553, AV726951, AV681618, AV706520, AV758668, BE048065, AV757455, AV710479, AI440426, BF726297, BF037097, BG114104, BG257535, BE047859, AL513693, AV755581, BG180996, AV756122, BF970162, AI340582, AI863014, AL036980, AL120854, AI349256, AL515173, BE887488, AI469532, AV681857, BF673434, BG178809, AV757797, AV762488, AI312152, AL515047, AI580190, AV757943, AI349937, AL514803, AV727776, AI673256, AV708119, AV733819, AV757737, AI934036, AV755290,

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6	HSCPT22	99	1209266	AA885943, AI807908, AI214900, BF813978, AV657190, AA018863, F31353, AI810745, AA725810, AA018896, AW450272, and H91431.
7	HTLED86	17	1253125	BE795173, BE396202, AI660332, AA203212, AA449065, AW328367, BF341164, AI392657, AV654528, AA813194, BF732391, BF115878, AI151232, AI291374, AI858223, BF515283, AI560253, BE857199, AW449943, AW083349, BF732290, BF513268, AI191781, AW166236, AA968918, AW006233, N27280, AA479498, AA628224, AA778607, AW104829, BF970270, AW182126, AI245640, AI269136, AI247510, AI738471, BF062346, AA402172, AI991306, AA411981, R70251, AW405094, AA883484, AW881569, T19278, BF306943, AI215021, AA018465, AA832117, BG027648, BF739796, AI825124, T95699, AI637616, AW001378, H01229, AA479495, R72487, AI767110, BF514171, AW889978, AA831289, AA922164, AA286916, BG001513, AI096849, AA962361, AA809942, R38228, C02128, AA831675, AI699011, AI308035, AW268060, AV743631, BG166999, AW302973, H42825, AI802826, AI612068, AI309420, AI539153, AI318254, AI570966, AI696969, AW409775, AI539632, AI365256, AI677797, AI698401, AI345787, BG165051, AI611418, AI360560, BE965724, AW088899, AI280661, AI537617, AI612759, BF726001, BE621256, AW102900, BF342341, AI784028, AW193203, AI680498, BE962865, AI366985, AW265004, AI468872, AV706775, AI950688, AI610667, AI348880, AI802240, AA603709, AW082594, AL120736, AI349646, AA493923, BE885353, AI590702, AI866082, AI633477, AI752007, AI866111, AW085639, BF814449, AI251221, AI472536, AI358042, AW827106, AI434242, AI349967, AI345615, BG260144, BE048087, BF921103, AI919345, AW858254, BF815196, BF915208, AW858243, AA974506, AI251205, AI829377, BF575118, AI339435, AI648502, AI445010, AW302073, AW262565, BF986689, AI952064, AI623363, AA999906, AI285586, BF924884, AI567637, AI697324, AI679550, BF317483, AI470293,

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7	HTLED86	100	1222077	BF732391, BF115878, AW083349, BE857199, BE396202, AA479495, AW328367, AA479498, AI858223, AI151232, AA778607, AW405094, BF514171, AW166236, AI291374, AI567943, AI560253, BE795173, AI096849, BF732290, AW449943, BF515283, AA628224, AI191781, N27280, AW006233, AA968918, AA761741, R70251, AW182126, AI245640, AI269136, AI738471, H00846, T19278, AA883484, AA286916, BF529836, AI660332, AW104829, AA018465, R38227, BF739796, BE905019, AW001378, H01229, R70296, AA831675, AI767110, AA832117, AW889978, AA831289, AA922164, BF970270, AA402172, AA962361, AA203212, AA809942, AA876230, BE882323, AW881569, R38228, BG027648, T95699, BF341164, BF986689, R72487, and AJ250392.
7	HTLED86	101	1221659	BE795173, AI660332, AW104829, BE396202, AA203212, AA402172, BF341164, AW328367, AW881569, T19278, BF970270, AA832117, T95699, R72487, AI858223, AI560253, AI151232, AI291374, AI245640, AI269136, AI738471, BF732290, AW449943, BF515283, AI767110, BF115878, AW083349, BF732391, BE857199, BF739796, AA968918, AW006233, AW166236, AW182126, AI191781, AW889978, AW001378, BG027648, AA831289, H01229, AA018465, N27280, AA628224, AA479498, AA922164, BF306943, AA778607, AW405094, AA962361, R70251, BG001513, AA809942, AV654528, AA883484, R38228, AA449065, AI392657, BF986689, BF514171, and AJ250392.

8	HTPKP89	18	1263310	AI681538, AA399973, BE326518, BE504079, AA573265, AA401309, AI379315, AI215506, AW471197, AI377132, AI681742, AI332991, AW269403, AI377465, AI685315, AA456746, AI263428, AI374952, N93369, N23006, N32714, AA884641, AI218150, AA226426, W24957, AI140445, N95585, AA773714, AA253264, T86889, H17820, AW269001, T86888, AA226563, AI033243, AA041235, AA358475, H17819, R16622, R16564, W25386, AA883664, AA773710, R16637, AA040797, BF509086, AW895164, AI927610, N89206, AI208762, AK027056, and AK026797.
8	HTPKP89	102	1213121	AA399973, H17819, AW895164, N89206, AI681742, BE326518, BE504079, AK027056, and AK026797.
9	HSRFP52,HJBCU75,HSRGW16	19	1254537	AA789332, BE669814, AW469963, AI925535, AI925543, AV728348, BE080915, BF732842, BE670545, AI685010, AI690167, AA570056, AA470465, AW969303, AW770920, AA311661, AI634463, T95424, AI283530, AW003925, AW080646, T95333, BG179881, BE617765, AI468303, BF310921, AA312696, AA347877, AA336623, AW268987, AW962841, AA356443, BF690832, AA311608, AA682679, and BE962309.
9	HSRFP52,HJBCU75,HSRGW16	103	745408	AA789332, AW469963, AI925535, BE669814, AI925543, AV728348, BF732842, BE080915, BE670545, AI685010, AI690167, AA570056, AA470465, AW969303, AW770920, AI634463, T95424, AW003925, T95333, AW080646, BG179881, BF310921, BE617765, AI468303, AA312696, AW268987, AW962841, AA356443, BF690832, AA311608, AA682679, and BE962309.
9	HSRFP52,HJBCU75,HSRGW16	104	1182209	AA789332, AW469963, AI925535, AI925543, BF732842, AA312696, BE670545, AI685010, AI690167, AA570056, AW962841, AA470465, AA311661, AW969303, AW770920, AI283530, AI634463, T95424, AW003925, T95333, AW080646, BE617765, AI468303, AA311608, AA347877, AA336623, AW268987, BE669814, AA356443, BF690832, AW753521, AA682679, and BE962309.
10	HDHEA83	105	1213580	AW971745, AW861944, AW804686, AW392670, AL119355, BE695785, AW604723, BF868687, AW858526, U46351, AW858525, AW877209, AL119319, U46349, AL119324, AL119457, AW577135, BE705903, BE705906, AW372827, AL119483, Z99396, AW384394, AW861889, AW858455, AW363220, AL119341, AL119497, AL119484, AL119363, AL119391, BF868697, U46350, U46347, AL119443, AL119418, U46341, AL119444, AL119399, AW604726, AL119439, BF868684, BE705905, AL119522, AL119396, U46346, AL119335, AL134902, AL042984, AL037205, AL119401, AL134536, AL134538,

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10	HDHEA83	106	1217946	AI816163, AI928507, BE778289, AW157769, AA115293, AW162106, AA059445, AW665627, AW139159, BG252118, AI192344, AI885801, AW665634, BF002221, AA865462, AI581151, AI674451, AW953263, AA190572, AI364132, BF059737, AI740781, AW157220, AI743998, BF739901, AI337924, AA993075, AI564803, AI400087, AW139120, AW340685, AW081568, BE858480, AI686640, AI271370, AI917170, AI379866, W07097, AA609367, AI827282, AI130691, AI022774, AI148957, BF224008, AA236262, AI494517, AA548108, AA045201, AI089708, AI123670, AI392976, AA748177, AA479158, W30860, AA977280, AA464601, BF434738, AI865643, R11725, AV694720, AA758679, AI910788, AA608963, AW770704, N68177, AI370751, AI634775, N79357, H64063, AI143918, N70018, N70101, D56114, AW292793, AI130031, BG054534, W76453, AI017785, AI332514, N89589, AI953179, T08704, W25482, BG112230, AA769968, AI361520, AW052056, AA253390, N93606, AA576801, AI419339, AI582942, AI141956, W00904, AA917660, AW952656, BF922214, BF922329, AI554648, BF922196, W44446, BF922198, W72167, AI926095, AI038178, BF922336, H23389, H17572, BE621053, N80636, AI024529, AW515684, AA253494, AA442642, AW160489, BF732739, AA490370, AI338291, AA775555, AI569707, AI240331, H10232, W44333, AA193686, AI873106, AI224568, AI768727, BF922191, AA147429, H80788, AA580142, H29283, H49657, R12178, BE829596, N94570, R64411, BE671020, AI743751, R11308, AI631146, H20219, R15108, AW611951, AI809025, AA064633, H21486, AA664481, T33459, N72328, T93973, AV722621, AA548109, R11692, AI123156, AA779540, H29372, H10188, R17698, AW028801, AA203687, AV684911, H58194, BE829585, R25302, BF194784, H64012, AI199446, AI970230, BF203288, AV688218, AI249347, BF922339, AV688252, H49578, AA621000, BF436352, R10906, AA479159, AV698634, BE816514, R52445, Z38875, AI369842, AW086460, H23278, R63805, N77929, BF476560, AI302454, H58195, T93297, AI470857, R61486, AA432390, AW052072, AW135183, AI338947, AI652083, R11309, Z42721, W07362, AI654228, H40308,

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11	HFXBR92	21	1243870	W01583, AA111937, BE839158, AA705807, BE839119, AL044762, Z30116, BE839157, BE838977, N55865, BF725844, BF827578, AW674277, BF827572, AW963444, AA456924, H29914, BF821009, AW161016, H38769, AA714011, AI279417, BG010084, BF792474, AU140208, AL041240, AV756491, BF725178, AI866580, BF821897, BF922071, AW023111, AA487226, AI569981, AA284247, F35684, AW674258, AI560085, AW275432, AW897697, AA714110, AA582746, AI187148, AI984168, AI282623, AV738383, BG222875, AI433104, AA171892, AW516255, AI799607, AV760091, BF198067, BG009504, AI362442, AB014513, AJ133768, AJ133767, AL049589, AF196779, AC006449, AC012467, AL009183, AC008392, AL137798, AC004797, AC007030, AC004980, AC009600, AP000310, AC018514, AC009247, AC011540, AC025588, AL117354, AP000116, AL109743, AL049636, AL117348, AC002350, AL157938, AL031848, AC003108, AC005098, AC005529, AC007637, AC004966, AL133387, AP000022, Z98044, AC005274, U63630, AC002347, AC018663, AP001426, AC003982, AC009244, AL136228, AC005837, AL050349, AL109614, AC007488, AF053356, AC002470, AC010422, AC004150, AC007365, U52111, AC002091, AB045146, AL109976, AC020916, AC024584, AC005846, AC006026, AL079335, AL133355, AC022436, AL049776, AC005052, AC006509, AC008753, AC002425, AC007066, AL008630, AL035400, AL160231, AC007686, AL022313, AL158198, AC007400, AL356299, AC005776, AL022163, AC005236, AL121886, AC006978, AL122002, U89337, AC007850, AP001731, AC004222, U95740, AC006966, AF129756, AC004166, AC004882, AC004832, AC007685, AC004694, AC005261, AC010458, AC011442, U80017, AL353804, AC003101, AC013447, AC009003, AC005071, AL133230, Z93024, AP000345, AC006330, AL135744, AB001523, AC008806, AC004983, AL049569, AC004383, AC009508, AF196969, AC008764, AC005189, AP001717, AL162831, AL121601, AL359382, AL138733, AC007201, AC007845, AL122023, AC083871, AC007226, AL008735, AL121751, AC005730, Z93015, AC007782,

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11	HFXBR92	108	1208739	BF725844, AW674277, AW963444, BF821009, AA456924, H29914, AW161016, BF792474, AA714011, BG010084, AI279417, AI866580, BF821897, AU140208, AL041240, AV756491, BF725178, BF922071, AW023111, AA487226, AI560085, AI569981, AA284247, AI984168, AI433104, H38769, F35684, F30158, AW674258, AW897697, AW275432, AA714110, AA582746, AI187148, AI282623, AV738383, BG222875, AV760091, AI799607, AI690497, AA171892, AW516255, BE138484, BF198067, AP000116, AL009183, AL117354, AC003108, AC018738, AC005919, AL135818, AC008044, AC004805, AP001714, AC002565, AL117348, AC008155, AC003982, AC005519, AC002543, AF190464, AP001717, AC009365, AC008543, AC006449, AC008760, AC005098, AC009086, AC010605, AP001709, AC004867, AL136223, AC005746, AC005080, AL163247, AC008736, AL109743, AC007030, AC004383, AL135783, AC004166, AL049589, AC005261, AF196779, AL137129, AC008403, AC007637, AC002477, AC009247, AC009600, AC011489, AP000310, AP001748, AB003151, AC018514, AC025588, AC011540, AC012467, AC008392, AL137798, AL161670, AC020552, AC007597, AC002045, AC005280, AC005920, AC004966, AC005237, AC009060, U89337, AC002485, AL109935, AL078461, AC006509, AL136305, AC002350, AL031848, AC007225, AC004797, AL162831, AC005529,

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11	HFXBR92	109	1046466	W01583, AA111937, AL044762, BE839158, AA705807, BE839119, Z30116, BE839157, BE838977, N55865, BF827578, BF827572, AA091640, N89082, AA249409, BE839162, AA425362, AA248041, AV727824, AV699224, AB014513, AJ133767, and AJ133768.
12	HSYIH77	22	1276392	AL524088, AL110452, AW749657, BF589432, AA280081, AW294123, AW149570, AW130349, AW055009, AI949814, AI142520, AI982810, AW161528, AA047100, BE855561, AL524089, AW157022, AA281323, AA101644, AA279077, AA938948, AW629474, AA485084, AA592999, AA101643, AA631312, AA775640, AA759272, AA047237, AI183353, AI374883, AW892064, AW073343, AA485196, AI081003, AL536073, BE185537, AA491277, AA482141, AI370489,

				AA331847, AI243704, AW613930, AW613943, AA757371, AI824149, AA897566, AI362091, AI243938, AA883065, AA745309, AA744016, AA744211, AB047883, and AK026237.
12	HSYIH77	110	1209388	AL524089, and AL536073.
13	HTAHS92	23	1243918	AW207577, BF092253, AI808825, AI122773, BF940077, AI360866, AA843394, AW162643, AW161798, BF055052, BF092246, BE856661, BG167100, AA465420, AI123189, AI031947, AI804220, AW975899, AV716838, AI472045, AA578830, AI740490, AL041924, AI075265, BF725844, AI873914, AA019973, BE395519, AI282253, AA013168, AW591276, BE139139, AI250552, AI223626, AI254770, AI249853, AI251284, AI251203, AI251034, AI284543, T74524, AW969743, AW975210, BF092245, AA515728, AI432298, AI283334, AI224956, BF805088, AI369580, BF725761, BE042006, N31708, AI251241, AI309059, BE968744, AA829036, BF880777, BE138387, AW338021, AW303098, AA483606, AI984168, AL079734, BG152773, AI687343, AA570740, AI754105, AA568204, AW872676, T96036, AI613389, BF857849, AL041706, AA054085, AI821200, AI755214, AW576251, AI754567, AI431513, AV743864, AW500684, BE328286, AV764001, H29914, AA533054, AW238341, AI634187, BF821897, AW069227, AV718585, AA485482, AA572983, AI801649, AI791659, AI864500, BE139133, AI889579, AW275432, AI744830, AI801563, AK026704, AC008760, Z97053, AC020910, AL078475, AC006509, AL163203, AP001621, AC006116, AC008753, AC018676, AC022143, AL049540, AC008083, AP001748, AC008892, AL121936, AC004025, AP001629, AC011749, AC018644, AP001745, AL163204, AC002059, AC002091, AC005996, AC000041, AC009424, AB035185, AC009410, AC007283, AL024498, AC006033, AC010135, AJ297357, AF165176, AL163283, AC003695, AF030453, AC078847, AC006040, AF117829, AF159056, Z93241, AC022148, AC005088, AP001660, Z98950, AC018633, AC004617, AC078899, AC005295, AC002992, AP001743, AL050308, AC005919, AL031602, AC006539, AP001347, AB019438, AL355980, AL133163, AC007276, AP001615, AL139277, AF064863, AC007690, X96421, AL136501, Z83839, AL355478, AC011449, AP001630, AC007193, AC004459, AC009276, AL117337, AB020859, AL356234, AF205588, AL022332, AL137861, AL139826, AL355101, AC005229, AC008969, AC007972, AC003682, AC007793, AK022963, AL031432, AL133258, AC007284, AL031846, AC004230, AL035461, AC010143, AC012039, AC006987, AC005901, AP001050, AP001751, AC008556, AL049646, AC022150, AC010326, AC004921,

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13	HTAHS92	111	1213187	AW969743, BF805088, AA483606, AA570740, AA568204, AW872676, AI613389, AI821200, AA485482, AL041706, BF725844, BF857849, BF885741, AW008317, BF821009, AA737158, AW872575, BF880777, AA021552, AA829036, AA664126, T49184, AI792304, BF821897, AC008760, AK026704, AC002036, AL138756, Z95114, AC005722, AC005514, AL159997, AC007563, AC005180, Z81364, Z98946, Z95152, AL162424, AC000025, AC011489, AC006449, Y10196, AL139100, AC000003, AC006487, AC011475, AL133448, AL031595, AL031597, AL049569, Z82244, AL137802, AC007375, AC012384, AP000555, AC005164, AF196969, AC003043, AF045555, X74558, AC005288, AC024947, AC008560, AC008687, AC010463, AC006064, AC005696, AJ277546, AL109827, Z98051, AC005529, AC004826, AC008403, AP001714, AC007541, AC009086, AC010412, AC011495, Z83856, AC005377, AC005081, AL162458, AC003957, AL357374, AL033529, AC005920, AF001549, AC008569, AL049539, AL031295, AP001718, AC007384, AC011490, AL133500, AC006285, AL133445, AL109798, AC009470, AC005746, AC004030, AC009516,

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13	HTAHS92	112	1042420	AW207577, AI075265, BF840301, AI873914, T96046, T96036, AK026704, AC008760, AC009410, AC018676, AC020910, AC011749, AC010135, and Z60397.
14	HAROV59	24	1272018	AL358532.
14	HAROV59	113	1209631	AL358532.
15	HDCCG73	25	1243884	AA730365, AI061294, BE154945, AP001715, AC004966, AL352979, AL118525, AP001671, AP001716, AC008556, and AP000404.
15	HDCCG73	114	1209263	AW975626, AW976024, AW973789, AW974658, AW970942, AW974806, AA730365, AI061294, AW979160, AW974986, AW971953, BE154945, AW973821, AW972440, AP001715, AC004966, AP001671, AL118525, AL352979, AC008556, AP000404, and AP001716.
16	HQAHD50	26	1243837	BF437711, AI817776, AI970996, BF476543, AI400849, BE645938, AI972893, AI762586, AA730695, AI201489, AW016419, AI799832, AI380706, AI675646, AI669800, AI658490, AI919017, AI418072, AI468338, BE645813, Z65567, and Z65568.
16	HQAHD50	115	1209703	BF437711, AI817776, AI970996, BF476543, BE645938, AI400849, AI972893, AI762586,

				AW016419, AA730695, AI380706, AI201489, AI799832, AI658490, AI675646, AI669800, AI919017, AI418072, AI468338, BE645813, Z65567, Z65568, AA121716, AA130776, AA146672, AA149359, AA416552, AA569970, AA290712, AA994552, AI312518, and AI187723.
17	HROBA16	27	1243878	BF834863, AA772704, AA577770, AW469214, R67262, AW160615, AL355094, AC004491, AJ277546, AC007193, AC024075, AC004983, AL365505, AC003982, AL080243, AL162430, AL354720, Z83840, AC009314, AC006483, AL132653, AC007404, AC004953, AC008736, AC008068, AC004477, AL050335, AP001748, AC004971, AC008403, AL137073, AL031005, AP000692, AL121753, AP001747, AP000347, AL031311, AC005520, AC002044, AC027319, AC004223, Z83822, AF038458, Z84466, AC012442, AC005668, Z83826, AL118520, U47924, AL022313, AC009086, AC016637, AC004743, AL035689, AL008582, AC009228, AC004655, AL133245, AC005355, AL031659, AC004448, AL353802, AL049776, AC007298, AC020663, AC009756, U80017, AF053356, AC011500, AC004150, AC016601, AC024561, AC005261, AC006334, AC006064, AC007312, AL121574, AP001725, AC007191, AC011445, AP001660, AC004531, AL031289, U95740, AL022323, AC083871, AC004967, AC011491, AL445220, Z85986, AC004000, AC004815, AC005004, AP000550, AL132639, AC004841, AC005519, AC005288, AC003029, AL138976, AC005971, AC005585, AC010326, AF168681, AC008018, AC004765, AC005372, AC010463, AL132713, AC011529, AC011442, AP001713, AC005839, AL139109, AC002425, AC007285, AL137802, AC005529, AC004257, AL121653, AC002565, AC011444, AL109804, AC007383, AC005103, AC004104, AL020993, AF047825, AC004882, AC007957, AL137853, AC010422, AL021940, AC005844, and AC016830.
17	HROBA16	116	1218577	AL355094.
17	HROBA16	117	1046802	BF834863, AA772704, AW160615, AA577770, R67262, AW469214, AL355094, AC004491, AJ277546, AC024075, Z83840, AC003982, AC004983, AC012442, AC004953, AL121753, AC004477, AC004967, AL132653, AC008068, AL035420, AP000692, AL050335, AL354720, AL118520, AL365505, AC007404, AC004971, AP001660, AP001747, AL035689, AC006483, AC009314, AL035405, AC008736, AC011445, AC006334, AC008403, AP001748, AL031005, AC005520, AC005844, AC004743, AC024561, AC010326, Z83822, AC011442, AC002352, AL022323, AC027319, AF038458, AL031659, AC007298, AL022313, AC004655, AC016637, AL049776, AC005668, AP000347, AL137073, AL008582, AL031311, AC009228, AC002044,

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18	HTPJD12	28	1262048	BF032776, AA492506, BE501761, AI380126, AW753589, BE742519, AA772096, AW959236, AI051248, AI796046, N78680, AW104821, AI923995, AW194429, AI082180, BF034807, AA468796, W86908, AA214384, W35375, N73147, W32940, AI640542, AW971155, W15186, AA294934, AW050468, R92821, T82084, AW170216, BF592081, AA211695, T81773, AI905700, AW837086, AA354566, AC007655, and AC083862.
18	HTPJD12	118	1209268	BF032776, AA492506, AI380126, AW753589, BE742519, AW971155, BE501761, AW959236, AA772096, AI051248, AI796046, N78680, AI923995, AW104821, AW194429, AI082180, AA468796, BF034807, W86908, AA214384, W35375, N73147, W32940, AI640542, W15186, AA294934, R92821, T82084, AW050468, AW170216, BF592081, AA211695, T81773, AI905700, AW837086, AA354566, and AC007655.
19	HHAWD13	29	1272864	BF926344, BF333687, BF743657, BG179438, AW630972, AW409772, AV717730, BE887537, AV713988, AV757469, AV717397, BE886223, AV713143, AV758017, BG171892, AV763927, AV715229, AV760840, AV760969, AV713908, AV717125, BE890608, AV713689, BE904681, BF365864, BE888844, BE908306, BF033687, BF034209, AA838230, BG031447, AV716915, AV762389, BG035988, AV757975, BF033366, BG113811, AV734800, BE905336, BE787806, AV715556, AV756771, AI440091, AA148136, BF726605, AW084248, AW023232, AI285434, AV713309, AW007955, AA579241, BG030733, AV758314, BF338493, AW950745, AV716133, AI972170, AV717021, AA679272, AI583929, W05480, AW118404, BG029162, AV733344, BG252807, AV716265, BG036404, AI075084, AV733451, AV716931, AI572892, AA633937,

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19	HHAWD13	119	1209632	BF365864, BF743657, and AW891104.
20	HISFI83	30	1243886	AW978652, AW271597, AI076921, BF056989, AI767684, AA429775, AA258066, AI922382, AI689445, AW517678, AW300599, BF382632, AI221849, N33450, AI243200, AW293699, AA258684, AW196901, AW001761, BE350684, N34663, AI889086, BF697102, AA278560, AA781749, AA279378, AA781748, AA505791, AW129213, AW957294, AA442866, N71815, AW953593, Z45035, AA709377, T74234, AA812710, AA352494, R63304, F12572,

				AA258589, AA442865, H00263, Z40767, AA852429, BE931765, AA852430, AI245143, AA954436, F05368, R63305, H00264, N44600, T88952, F10188, F01620, AA642668, AI088408, BE218685, AV702722, and D87455.
20	HISFI83	120	1209270	AW978652, AW271597, AI076921, BF056989, AI767684, AA429775, AA258066, AI689445, AW517678, AW300599, AI922382, N33450, AI889086, AI221849, BF382632, AI243200, AA258684, AW196901, AW293699, BE350684, AW001761, AA781749, N34663, AA442866, AA781748, AA278560, BF697102, AA279378, AA505791, AW129213, AW957294, AA812710, AW953593, N71815, Z45035, T74234, AA442865, AA709377, AA352494, R63304, F12572, AA258589, H00263, Z40767, AA852429, BE931765, AI245143, AA852430, AA954436, F10188, F05368, R63305, H00264, T88952, N44600, F01620, BE218685, AA642668, AI088408, AV702722, and D87455.
21	HISFV70	31	1253160	AI539118, W20054, AI866754, N91453, AI143495, AW383130, AA195793, AI378995, AL514765, AW827289, AW372903, AI627985, BG029829, AF119896, AL133016, U80742, AF116602, A65341, AK026648, X99257, AK024538, S78214, AL122050, AL137459, S56212, AF116639, AL049466, E03348, AK026086, I33391, AF130092, AF188698, and S68736.
21	HISFV70	121	1209259	AI539118, W20054, AI866754, N91453, AI143495, AW383130, AA195793, and AI378995.
22	HNSAB41	32	1268184	BE739592, BG165006, BG105699, AV690200, AV692456, BF666897, BF696358, BF697847, BE891061, BG165370, AV686169, BF666680, BF967755, BF696365, BF666285, BF029934, BF698234, BF700761, BF696359, BF698503, BF698021, BF667900, BF666952, BF665797, BF593954, BE958612, BE958515, BF668554, BF439364, BF670202, AW613123, BF699229, BF664617, BE958087, BF700926, BE739347, BF381642, BF669635, BF695972, AI569980, BF032034, BF697105, BE958350, BF542034, BF665003, BF382058, BF701837, BE958295, BF246840, AI753956, AW779376, BE536963, BF700216, AA554040, BF967109, BF246687, AW583705, AI580191, BE567846, BF695871, AI864614, BF669697, AI922513, BF695585, BF195797, BE959288, BG104703, D60241, AW663134, AA566088, H48650, AI682800, AA595575, AI453646, T50769, R68048, BF131792, N63391, T50929, C15568, D60751, R32457, C15261, D81750, D81691, R24902, H48485, BG104876, BF700708, AA155685, AK027169, and AB041548.
22	HNSAB41	122	1212804	BE739592, BG165006, BG105699, AV690200, BF666897, AV692456, BE891061, BF696358, BF697847, BG165370, AV686169, BF666680,

				BF967755, BF666285, BF696365, BF696359, BF029934, BF665797, BF698234, BF667900, BF698503, BF698021, BF700761, BF666952, BF593954, BE958087, BE958612, BF665003, BE958515, BF668554, BF439364, AW613123, BF699229, BF664617, BE958350, BF700926, BE739347, AI569980, BF697105, BF542034, BF700216, BF246687, BF382058, BF381642, BE958295, AI753956, BF670202, AW779376, BF032034, AA554040, BF967109, BE536963, BF701837, BE567846, BF669635, AI580191, BF695972, AI864614, BF669697, AI922513, AW583705, BF695585, BF195797, BF246840, BF695871, BG104703, AW663134, BE959288, AA566088, D60241, H48650, AI682800, AA595575, AI453646, T50769, R68048, BF131792, N63391, T50929, C15568, D60751, R32457, C15261, D81750, D81691, R24902, H48485, BG104876, BF700708, AA155685, AK027169, and AB041548.
23	HOCNY94	33	1278041	AW953965, AV655645, BE018334, BF342070, BF792146, AV703695, AL040243, AW301409, BG260037, BG179993, AL135661, AW087445, BG058398, BF792469, AI497733, BF726198, AI802542, AI318280, AI702406, AI269205, AI811344, BF794994, AW827203, AL044207, AI610645, BF344652, AW103371, AV681759, AL043326, BG112879, BF971016, BE874133, AI690426, BE781369, AI281762, AL121328, AW129202, AI799199, AI580984, BG151247, AL513907, AI440239, AI249257, BG031815, AI682841, AI912866, BE048071, AI538716, BG120816, AI857296, AW002342, AI612913, BF038106, AI539153, AI564719, BG036846, AI868831, AI633419, AI625079, AI682720, AW026882, AW274192, AW071349, AI620284, BF812933, BG058208, AW071417, AV681987, AI439087, AI872074, AI433157, AI284020, AI678302, AI568870, AI499463, AI636445, AW118512, AW131954, AI539771, AW196141, AI554484, AI866608, BF724691, AI281779, BF055737, AW183130, BG168696, AI475451, AI569616, BG180996, AI702433, AI224992, AW827249, AV681951, AI950664, AL513911, BF673434, AI498579, AI866002, AL048871, AI433976, AI884469, BF970446, AI445025, BF795712, BE963035, BF343172, AI800453, AW104724, AI800433, AV756122, BF525438, AV755668, AL119049, BE963918, BE881061, BF344479, AL047763, BG253026, AW169653, BF965836, BG164371, BF725868, AW238730, BE047952, AI888953, AI828731, AI921379, AL036146, BE894455, AI271786, AV757943, AI590120, BE018711, AW169671, AL121270, BF812961, AL036396, AI612920, AI610756, AI635461, AI570384, AI349004, AL513837, AI440426, AI250293, AV755207, BF883916,

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24	HAROG72	34	1281478	BG030787, BF342483, BE777852, AF062713, AW962150, AV762135, AV712960, AV725819, AA306731, AW247858, AI052532, AV716692, AI278003, AV723548, BE047593, AI887776, AV728257, BG026292, AW148694, AW898553, AA034516, AI168715, AW630982, AI191223, AW304793, AA025373, AI810804, BF798240, BF984626, AI792362, AA025374, AW051344, AA962385, BF957364, BF958687, AA132199, AA029525, AW439563, AA536183, AW474986, AI567232, AA029460, AI088927, BF928249, AW879285, AI457389, BF760131, AU147226, BF826830, BF828714, W87430, AA251931, AI806055, AW102811, BG260565, AI885218, AV762783, BG028665, AA974092, N28450, AL138265, BG109399, AW021737, R99679, AW886566, AW089550, AW118108, AA565273, H82553, AV733710, H49190, AA534064, AI452969, AI239787, AU148007, AA634991, AA694128, AU145476, H43461, AW157180, AW131249, BF840910, AI147206, BF738001, AW967632, AI791864, H99688, AU140392, U25759, AI433104, AI583978, AV727816, AL041013, AV760723, BE155132, AU157011, AA973562, AU148853, H27161, AL134691, AA782322, BF894632, AW963982, BE148835, AA864439, BG010084, BF930994, AA287618, AC024563, AL121881, Z95114, AC022148, AC005228, AC004047, AL138715, AL163202, AP001464, AL031683, AC006017, AL121958, AF205588, AL117339, AC009296, Z86064, AL022318, AC004006, AC004112, AL139350, AL356801, AC027689, AC009318, AC002386, AL136438, AC020728, AL008729, AC005010, Z98304, AC006484, AC006007, AC007099,

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24	HAROG72	124	1209767	BF871137, AW970877, AA457070, AV739452, AA493708, AI733856, AI473475, BF814725,

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25	HDACT07	35	1280454	AL514243, AL528669, BE727059, BF960481, AW387524, AI936906, AW965563, BF217740, AI571397, AA488594, AI803613, AI214239, AI417396, N50028, AW338022, AA235147, AI823751, AI368040, AA992177, AA421340,

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25	HDACT07	125	1209253	BE873056, AA251487, BF359951, AA233350, AW965563, BE891454, AU127479, T08369, BF571574, BF372580, AA301138, AA319705, BG009919, BF371427, BF813682, BE882092, AA972005, BF922373, BE727059, and AK022823.
26	HLTIJ80	36	1034753	AC004507.
26	HLTIJ80	126	1046031	AW772231, AI628760, and AC004507.
27	HNTZG72	37	1246154	BE075065, AI753488, AV758870, BE043920, BF885741, C06046, AV760469, C18083, BG222269, AF196969, AC005081, AL023553, AL021918, AL121926, AC012446, AC001228, AC008745, AC003108, AC006441, AC005324, AL096840, AC004913, AL136969, AC011500, AC011462, AC004707, AC006965, AC005527, AC011495, AC000025, AC004914, AC083875, AC005778, AL157713, AL020993, AC004526, AL109897, AC008848, AC005231, AC008392, AL008582, AC004150, AC005553, U07561, AC002553, AC006312, AC010150, AC012627, AL117382, AC004475, AC068799, U95742, AL031255, AC005225, AC007240, AF001549, AL022302, AL135749, AL022165, AL356244, AC010326, AC004922, AC009314, AL023284, AP000349, AL136231, AC008379, AL133174, AL356299, AP000509, AC016995, AF243527, AL161905, AL353807, AF217796, AC005488, L48038, D84394, AC008372, U52112, AL096701, AC005529, AL078644, AL353194, AC010291, AC007850, AP001711, Z99716, AC026439, AC027319, AP000961, AC009301, AC005829, AC005046, AC004703, Z73417, AC000026, AL121891, AL117336, AP000555, AC005512, U47924, AC011491, AL161938, Z82178, AC008892, AC008521, AC011444, AC004965, AL031666, AF045555, AC007731, AC004765, AC006064, AF010238, AC005670, AL096791, AC006160, AP001725, AL136179, Z94721, AL031680, AC005500, AC002472, AC007277,

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27	HNTZG72	127	1209378	BE075065.
28	HNUCE33	38	1275160	AL047045, AI810840, AA453163, BG105390, AI384012, BF675676, AI580098, AA847601, BE465717, AV702308, AI743043, AI140310, AI275910, AA496037, AW169938, AW302619, AI990162, AI683202, AA976888, AA235887, AI080761, BF105912, AA292967, AA947702, AA398374, AI915809, AA236971, AI679067, AA861155, BF690995, BF673125, AI187078, BF671654, AA644201, R71690, AW769518, AI831892, AI334002, T94071, AI205587, BE697944, AI799793, BF671393, AA397540, AW841936, BE697973, AW591306, AI286327, BE928278, R45381, AI919197, AA904036, Z25172, BF810391, BF436497, AA009755, BF084095, AW968019, AA009646, AI247693, R49618, AI222632, BF027853, H17649, AL047044, N35425, D45539, BF991093, F09385, T94148, Z40038, BF446066, AW582847, BE161358, AI628827, AW879374, BE832740, AW994806, AW879360, BE832690, AA779150, BE150929, AW879368, AW879442, BE832676, BE832651, BE832724, BE832745, BE832646, BE832749, AW879378, BE832743, BE832680, BE832691, AW879371, BE832649, BE774568, BE832728, AW879444, AW879351, AW879366, BE832726, AW879347, AW879293, BE832721, AW879333, AW879348, AW879359, BE697941, AW879439, AA252673, AW879399, AW795305, H17765, BE832688, AW879473, BF790133, BE810268, AW879349, AW879441, AW008391, AA613997, AA435878, AL514473, AI619502, AL514087, AI862139, AL514791, AI564719, AI270183, AI274013, AI632851, AI572787, AI677796, AL514357, AA507158, AL514983, BE966388, AL513907, AW169527, BF526526, AI889376, AI538085, AL513999, AI824557, AI289937, AI476046, BF904265, AL513901, BF812938, AI869367, AL513977, AI680498, AI434468, AL514691, AL513807, BF812961, AW075413, AI274508, AI538716, AL514627, AL513553, AI433157, AI702073, AL513911, BE965891, AA449768, AI569583, AI799199, AI926790, AW879354, BE967261, AI567351, BG181066, AL513693, AW075667, AL514093, AW029611, AI636719, AI273964, AI863321, AW104724, AI280747, AI366900, AW102785, AW190042, AI699865, AI554821, AI630928, AL514823, AI634345, AI271786, AL514359, AW149869, AI873644, AI247293, AI569328, BF970652, BE966577, AL513779, AI287326,

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28	HNUCE33	128	1209149	AV753557, AL047045, BG164060, AI810840, AA453163, BE612569, AW968019, BG105390, AI384012, BG121257, AW162396, AA436948, AI580098, BF675676, AA732323, AA847601, BE465717, AW295116, AV702308, AI480288, AI140310, AI275910, AI743043, AA496037, AA461195, AI703240, BF671654, BF690995, AW169938, AA009645, AA009755, AA397540, BF105912, AW302619, AI683202, BF027853, H17765, AI990162, AA976888, AA235887, AI080761, BF673125, AA292967, AA947702, AA398374, AA236971, AI915809, AL047044, AA861155, BF810391, AI187078, BF671393, AA252673, AI094148, AI915790, AI679067, AI246899, R71690, AW769518, AI831892, AI334002, AA644201, BF790133, AW172420, AI205587, T94071, AI799793, BE697944, N35425, AW841936, R68928, BE697973, BE890287, AW591306, AI286327, Z43980, BE928278, AI919197, AA904036, R45381, AW008391, Z25172, R34745, R21290, BF436497, F11727, BF084095, AA009646, AI247693, AI222632, BF833775, R49618, H17649, W32783, D45539, BG178952, AW393390, BF991093, F09385, T94148, Z40038, BF446066, AW582847, BF910900, BF886363, BG152273, BG152272, BE161358, AI628827, AA779150, AW879374, BE832740, AW994806, AW879360, BE832690, AW879368, AW879442, BE832651, BE832676, BE832724, BE150929, BE832745, AA613997, BE832646, BE832749, AW879378, AW879371, BE832743, BE832680, BE832691, BE832649, BE774568, BE832728, AW879444, AW879351, AW879366, BE832726, AW879293, AW879347, BE832721, AW879333, AW879348, AW879359, BE697941, BE222367, AW879439, AW879399, AW795305, BE832688, AW879473, AA521309, BE810268, AW879441, AW879349, AW138831, AA435878, AA984310, AA507158, AW879354, AW879434, AW879476, BE243176, BE855524,

				AF293366, AC008176, AC006987, and AA883799.
29	HODEM32	39	1253127	M62006, AL036896, AA610381, AW151541, AA669238, AW974363, AL041375, AL041924, AW265468, BG180320, AL121039, AI702049, AI754926, BG110480, BE273825, AI254267, AV759766, AW148821, AA832175, AW410844, AA489390, AI797998, AW270468, AV761486, AU157209, BE501670, AI473671, BE161469, AA298365, AW020198, AW151848, N92588, AU146487, AA814503, AI547110, AW084445, AI284543, BF828756, AA425283, BG059139, AV732057, AI572680, AI336771, AV710119, BE139139, AI250552, AW243808, AV758870, AL042735, AA729387, AI889995, AV730440, AU160445, AW162314, AI251284, AI251203, AI251034, BF965370, AW593631, AI914748, AI270280, AA604601, AC005233, AL021877, AC004453, AC005538, AL390039, AL355497, AL034548, AC007030, AC005323, AC005678, AP001719, AC005726, AC006487, AL137784, AL121865, AF111167, AC008555, AC007676, AP001684, AL133396, AL157931, AL023574, AC002091, AC007883, AC007684, AC005048, AL049594, AL136981, AC017006, AL049823, AL024498, Z98745, AP000359, AC004125, AC005243, AL354889, AC006948, AC004673, AC005998, AL353788, AL121983, AL135787, AL158040, AC005369, AL358975, AL109759, AC005288, AL353140, AP001628, AC004041, AC006080, AF011889, AC004106, AC007632, AC006376, AL078645, AL031650, AC022073, AC011479, AP001747, AC026881, D87675, AL137129, AL359272, AL355980, AL136452, AC024154, AC005207, AC006581, AP001695, AL133240, AL121593, AL022345, AC005188, AF111168, AL163302, AP000142, AC007748, AJ400877, AB026898, AL009172, AC005696, AC004185, Z93928, AL163282, AL031665, AC007308, AC004089, AC005899, AC008806, AL031311, Z93015, AP000509, AC008372, AL031666, AL080243, AC005069, AC008543, Z93020, AL022318, AL049856, AL158817, AC007546, AF238375, AC007371, AC008394, AL355385, AC011495, AC017002, AC005080, AL121656, AL121914, AC006143, AC073934, AC008569, AF205588, AC069277, D84394, AC007881, AC025588, AL139109, AC011442, Z84469, AL109976, AC018642, AL031255, Z98950, AL139396, AL157838, AL034422, AC004383, AC003982, U91327, AL117330, AL391867, AC008379, AC027644, AJ003147, AL035400, AF254822, AL133480, AL445483, AC007993, AC011497, AC005484, AC024576, AC005920, AC005274, AL360227, AC004881, AF109907, AF067844, Z98200, AC007954, AL139353, AC006064, AC005332, AC006006,

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29	HODEM32	129	1212873	M62006, AC004070, and AC002412.
30	HPJHQ20	40	1261918	BE883488, AC009518, AF035397, AJ009961, AC007682, Z17254, and AB034604.
30	HPJHQ20	130	1209298	BE883488, AC009518, AF035397, AJ009961, Z17254, and AB034604.
31	HQADO95	41	1276422	AI880874, AI080618, AV758790, AW131249, AW055226, AI523839, AW089550, AI919265, AU119532, AV756491, AI038990, BE393367, AL119123, AI654285, AC003665, Z98743, Z99916, AL109984, AP001672, AL096821, AL357153, AC004659, AL137067, AL034395, AC002553, AL355305, AC003664, AC007225, AC002045, AC009492, AC009481, AC005233, AC023425, AL021069, AL133246, AC004106, AL161797, AC010169, AC004016, AC006350, AC005034, AP001710, AC007344, AL049780, AC004963, AC008269, AC008753, AC006116, AC005874, AF134471, AL049834, AC008733, AP000048, AL035696, AC006042, AL139353, AC006948, AC005730, AC005070, AL354852, AC004626, AL163279, U91323, AC005274, AL138740, AC004526, AL035067, AC009313, AC009194, AL034411, AC002303, AC004824, AP001688, AL391122, AC007358, AL032822, AF064861, AL022332, AL021940, AC008155, AC005697, AC083874, AL031846, AP001700, AC007955, AC007938, AP001667, AL049742, AC012309, AL008709, AL096764, AC005411, AC023430, AL024507, AL035089, AC005082, AC003009, Z82899, AC020908, AC000065, AC001228, AL035697, AC066590, AL117341, AL049832, AP001708, AC010789, AC005295, Z93241, AP000246, AL391839, AL353771, AL031407, AL157694, AC002351, AC023796, AL109928, AC008543, AC022596, AC009116, AC004820, AL139383, AP002534, AL353804, AL117186, AL359238, AL133405, AC006530, AL163218, AC005971, AL139343, AC008038, AP001685, AL078602, AC007364, AC005548, AC007383, AL022395, Z95116, AL136139,

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31	HQADO95	131	1209746	AW963750, AL042853, AI306191, AI305894, BE907585, AW089101, AI674174, BE277210, BG113106, BE276480, AV733830, R44116, AI470646, BE409047, BF030591, AW023149, AW960545, AA468022, AL515875, BG002349, AV759279, BF343686, BF197650, AA846952, AV761211, AI421841, AI309375, AI751216, AV761104, AW886681, AI254913, AI281730, AW979252, F05324, AI333016, AI950983, AA468131, AL133294, AC011489, AC007193, AL135839, AL096702, AL035662, AL136169, AC007682, AC009784, AL158067, Z81310, AJ009615, AC002089, AC003658, AL031295, AC002301, AL031055, AC008101, AL137794, AC022308, AC008079, AL392084, AC073539, AC009481, AL158040, AL008709, AC004743, AL136131, AL158218, AC008249, AL022329, AC004971, AC023510, AP001212, AC003691, AC012598, Z83826, AC008958, AC026430, AL078461, Z97181, AC007350, AL023284, AC022543, AC003101, AL024498, AC007327, AC009756, AL133387, AC009311, AB014078, AC004209, AC006139, AL031575, Z97196, AC006468, AP000514, AL450226, AC006344, AC004592, AP000697, AL034351, AC002430, AL137039, AL022336, Z98884, AC020755, AC007263, AP000688, AC024162, AC026197, AP001726, AL163248, AK027088, AL024508, AL035415, AC005180, AL109823, AC002460, AC002195, AC005701, AL139112, AL035455, AC005768, AL031427, Z93023, AC005725, AC002383, AL136306, AC007488, AC007400, AC008394, AC011482, and AL031054.
32	HTENS88	42	1243927	BF512513, BF698790, AW119226, BF791196, AW500203, AA885462, BF349766, AA594588, AI821697, BE146008, BE709669, AI968693, BE738929, BF132258, AI690891, AA490875, AA810000, AI221437, AA737278, AA707477, AW300795, AW576517, AA827071, AA490949, AA831539, AA810785, AI472106, AA826937, N66975, AA482274, AA423813, AI613477, AI800856, AU145366, AA166655, AV728911, BF209807, AA680043, and AK021725.
32	HTENS88	132	1213009	AW500203, AA594588, AI821697, BF512513, BF698790, BF791196, and BF349766.
32	HTENS88	133	1045824	BF512513, AW119226, BF698790, AA885462, BE709669, AI968693, BE738929, BF132258, AI690891, AA490875, AA810000, AI221437, AA737278, AA707477, AW300795, AW576517,

				AA827071, AA490949, AA831539, AA810785, AI472106, AA826937, N66975, AA482274, AA423813, AI613477, AI800856, AU145366, AA166655, AV728911, BF209807, AA680043, and AK021725.
33	HTLGC03	43	1261928	BF732494, AI198873, AA861238, BF732473, AA927155, AA906741, AL036187, AI656448, BF344691, BF343568, AV682654, AL048656, BF817402, AI868204, BG256090, AI494201, AI251221, BG122481, AA807088, AI434833, BF812933, AI805769, BE621256, BG168696, F36859, BF038804, AV706987, AW149227, BF061283, BG178911, BG112718, BF904189, AW163823, AA287231, AL110306, AW235745, BE968711, BF924882, AI433034, AI929108, BG118829, AI582871, BE781369, AW963224, BF885675, AI280670, BF814357, BE620444, AI566724, AW274355, BF909758, BG253026, AA613907, AA761557, AI866741, AW813006, BG113299, AL036403, BE965121, AA493923, AA635382, BE048087, BG110660, BF920893, AW403717, BE964078, BG110259, BF924884, AI932949, AW059828, BE886728, BF344652, AW074993, BF812938, AI349614, R40432, AI863321, AW071380, AI874151, AW169234, AI343059, AW172723, AI312152, AV647118, AW075084, AW131930, BG058039, AI499285, AI349933, AI310925, BF340889, AV682466, BE965621, AI349937, BE621472, AI680498, BF726207, AW858254, AI922577, AW169604, AI307708, BG253206, BE544111, BE880085, AI866082, BE538466, H89138, AI620093, AI573026, AI254727, BF814541, AI345608, AI699011, AI307520, AI889147, AW088903, AW151714, AW129230, AA580663, AI538342, BF814453, BE965192, AI348854, AI307446, AI345677, BF032768, AI539771, AI872910, BF970186, BG107576, AI468872, AI866608, BF751710, AL120853, BE874133, BG168185, BG031664, BE964812, AV656932, AI805688, BE965481, BE789764, AI684021, BG105800, AI888621, BE966699, AI345471, BG251872, AI582483, BF904265, AI366992, AW068845, BE964497, AI886181, AI567582, BF092710, AI801325, BE967255, AA494167, AI174591, AL046463, BG105110, BE897632, BE965432, BE885490, AW168031, AW020095, AI400725, AW148356, AL037030, BG166654, AL120254, AV717349, AW129271, AW827227, AI539687, AI345347, BF753056, AW302965, BF213155, BE785868, AA640779, AL047387, AW162189, BF826445, BG029053, BF990285, AW827276, AI371228, BE172689, AI802240, AW073697, BF038131, AL036904, AL037558, AV738991, AW151681, AI471361, BE622183, BG058150, AL036631, BG029829, BG121959, BG001235, BE964636, BE904051, BE965355, BE909398,

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33	HTLGC03	134	1212925	BF732494, AI198873, AA861238, BF732473, AA906741, AI656448, and AL034550.
33	HTLGC03	135	1227183	BE277178, BF980634, BE732783, BE744869, BF205108, BE734231, BE902466, BG178169, AL043038, BG171519, BE298431, BF205706, BG107935, BE793662, BE537334, BF794278, BG035960, BE408797, BF307828, AA772073, BF983678, BE386724, AV734233, BE909061, BE251754, BE908982, BE734758, BE881757, BE908194, AA421156, BE884675, BE252692, BE379030, AV733932, AW263208, W07591, BE742898, AI860213, BE813829, AW438684, AA427665, BE272664, AW467358, AA397954, AV740176, AW778811, AJ403113, BG167807, AW675564, BE732299, AI348480, AW068454, AW004828, AI129055, AW327370, AW070768, AW769032, AI800035, R42232, AW249080, AW081957, BF307853, R15335, AL041293, BF032935, AI520752, AI695650, AI206299, BF366342, AA935849, AA204944, AW248645, AW769340, AW263189, AI656757, AW769555, AA342016, AA035137, AA576268, BE540445, AA293754, AA361461, AW573223, AW135932, AW672887, BE794930, BF737443, BE409559, AA330688, AA503645, AI917771, AA342017, BE867818, BE737487, BE892849, BE279770, BE275640, AI421042, BE252711, BE900859, BF366402, AW007750, BF988458, BF856355, BG151170, AK026991, and AL136295.
34	HTLKQ55	44	1243896	AI203269, AI916973, BE045921, and AW846714.
34	HTLKQ55	136	1213423	AW846714.
35	HTOJF42	45	1261944	AW081398, AW327868, AW972312, AV764314, AW339568, AI801600, BF724372, AW769399, AI350211, AI357551, AI431303, AA469451, AI471481, AI824562, AL046409, AV755070, AL120502, AI284640, AI358343, AV761403, AW265009, AI610376, BG059869, AA557686, AA491814, AA714453, AI061334, AW498486, AI859251, BE047069, AW962044, AW193265, AU147800, AA513181, AI761471, AV719506, BF668217, AV759204, AI053672, AI963720, AW833898, AI635818, AA608616, BE042649, AI669453, AI143242, AI889923, AI801591,

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36	HTPHC19	46	1284768	AV760623, AA431025, AW600282, AW600279, AI557017, AA737255, AA768281, and BF571514.
37	HDPHG50	47	1268191	AI692675, BE222314, BE147139, H06337, BG150512, F11466, AA887391, AI621341, BF995171, AW163394, AI927233, AI564398, AI474646, AI623941, AW051088, BF184134, BG025897, AV681864, BF982265, AI918809, AI918449, BE904851, AW983783, AI536923, AW410259, AI950892, AL531436, AI872118, BF925729, AV682190, AW073996, AA648480, AI612913, AI860027, BG108189, AV756451, AI432507, AV734425, AV732976, AV714341, AV733869, AV681884, BG113863, AV758146, AV757205, AV757362, AI439664, AV733824,

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37	HDPHG50	139	1213570	BE147139.
37	HDPHG50	140	1144654	AL531656, AL531655, AL523800, BF341028, BF339842, BG167581, BG164303, BE737156, BF341038, BE908879, BF342686, AU139779, BG260316, BF343615, AU139397, AI302100, BG257913, AU147880, AI741706, AI820002, AU148067, AW957065, AA772063, AU147303, BG165749, AI669059, AI833004, AI809858, AA613856, AU157378, AA147601, AI870387, AA975340, AA973040, AA610202, AI816754, AU157433, AW582946, AW275866, AI355268, BF435132, AI128083, AW137856, AW025018, AI340209, N29612, N25467, AI355997, AA522616, AU157679, BF341352, AI818337, AI624114, AU157053, BF940850, AI800730, N24047, AI801451, BF742275, BF994357, AA862639, AI240015, AI766024, AW168554, AW029568, BG056582, BF061533, AU157329, AI921514, AI570362, AV685526, AU158214, AW029522, AW511826, BG236804, N41612, AU157997, AU155872, AW262039, AI932807, AU156343, AU157956, BF475463, AU156117, AI089367, AU156451, AA452987, AU157115, AI521638, AA975021, AW583152, AA933839, AI431246, AV750535, AU155718, AW264924, BE046385, N55269, AU158010, AA903723, AI184811, BF154683, AU157041, AI560714, AA149236, BG056837, AW952172, AW025224, AW339117, AU155652, AI239967, AU156656, AA452847, BF342427, AI376060, AI432072, BF111546, BE247228, AI282593, AA148923, AI248238, R73038, R73039, AW193421, BF991003, AV686621, AA436817, AW881184, H46397, AI207313, AI288275, BF942463, R76226, AA329182, AI291769, AA149235, AA127914, N35867, W73313, BE246062, BF847661, AV751162, F25704, H45919, AW583296, F33694, AA738370, H50617, AA366267, BE871527, BG236861, D31336, AA987641, BF358443, AW243129, T83871, R76225, F16325, AI240532, R33363, H27296, R26702, H27107, AI368376, R01103, AA148922, AA320502, AA147746, R26925, BG002497, AA961249, D12414, D12442, AI919360, AA442573, R39563, R01835, F00836, T40026, N31508, AI832863, AA368870, N76878, BF740085, AA502640, AI380175, AI269372, AW882139, AI635861, AI707932, AI702513, AI624470, AW584015, AA368869, BE826061,

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38	HHEWS13	48	1243859	BF331658.
40	HPJGT38	50	1209290	AL118513, AL009181, AL109623, AC002302, AC008738, AC021036, AL022316, AC007192, AC011445, AL133353, AC008521, and AC011475.
41	HTFMK11	51	1276752	BE620294, BE620828, BE503158, AI718991, BE467982, AI749303, AI707929, BG149952, BE674357, AI434977, BF511462, R98920, R98694, AI668979, AA082389, AI114869, AI251284, AI251203, N57681, AI628859, AL037856, AI251034, AI917132, BF868994, BE139139, AI744830, AI250552, AA704393, AI284543, BF772474, BE062478, T57767, BE062476, AI223626, BF751949, AI254770, AW575000, BE878926, AA622479, AA715814, AV731013, AV742175, BF526832, AI609972, AW410354, AW270433, AW965633, AI610360, AW238253, AA427636, BE350953, BE042006, BF854308, AW576081, AL537142, BE301584, AV760508, BF991881, AV758067, AA158549, BF527070, AA714011, AA719433, T40388, AA836552, AI192440, AW516255, AW957372, C06004, AL133153, AC006967, AC004025, AL161670, AL022151, AF117829, AF131216, AC023347, AL137159, AC024085, AP000079, AC007029, AC004003, AL138735, Z98742, AC005235, AP001746, AC005939, AC007558, AC008774, AL031055, AC006013, AC013246, AC005015, AC004891, AP000080, AL161936, AL357519, AC004125, AC006457, AC004965, AL033375, AL121947, AL353643, AC006017, AC019172, AL159986, AF001549, AC009302, AL049825, AC005375, AL445465, AC009429, AP000081, AC004106, AC007739, AL096703, AC006348, AL133467, AC007364, AC004682, AC002418, Z83827, AC009492, AC004386, AL162377, AC017093, AL031726, AC007401, AC005486, AL034377, AC016601, AL137000, AC006512, AF245226, AL163206, AF108083,

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41	HTFMK11	142	1212928	AW974663, AW972226, BF526832, AW976003, BF751949, BF751953, BF751948, R97336, BF725884, AW973814, AW505476, AA985391, AI744306, BF918036, AW575000, AW103406, AV754364, AI891070, BF984807, AU147851, AA583394, T40388, AI537458, BF854308, AL023284, AC005914, AC020955, AL442167, AC006077, AL096840, AP001208, AL163285, AL031651, AL133545, AF225899, AL138820, AC004962, AC004884, Z98751, AF047825, AL096701, AL132642, AC005379, AL133415, AF002223, AC015973, AF111167, AC003950, AC016601, AL138889, AC008403, AL137802, U95739, AC008033, AC002350, AC005694, Z82194, AC004089, AC000070, Z83822, AL049692, AC009756, AC005103, AC005544, AC005952, Z99716, AC005377, AC005971, AL132855, AL117382, AC083862, AC009247, AC004458, AP001725, AC026431, AL022165,

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41	HTFMK11	143	1042907	BE620294, BE620828, BE503158, AI718991, AI749303, BE467982, AI707929, BG149952, BE674357, AI434977, R98920, R98694, BF511462, AI668979, and N41718.
42	HTSGQ95	52	1280458	BE738386, BE618898, AL537582, AW168786, AI891062, BE795754, BE378973, BG236152, AW006340, AI963319, BE675855, AW375108, AI422309, AL536577, AI832931, AI817124, BF973736, AI970605, BG248399, Z99384, BF683882, BF344063, AW955744, BG179903, BE881482, BE208231, AW874353, BE410944, BE267254, AI678964, AI884862, BE871137, BF027496, AI817815, F26345, BE277273, AA860159, AA989510, AA604546, AW751837, AA460040, AA808442, AI421161, AI198659, AW517816, AW951654, AA703967, AI223227, AA826439, AI300856, AA496882, AW873936, BF946448, AW663377, N94113, BE733872, F22350, AW631193, AA134976, AA701063, AA588881, BE906580, AA668703, W21804, BE873571, AW751838, BF027022, BE936810, BF313568, BE790976, AA459951, BE796767, BE562126, BF313746, BF973015, AI673415, AI272103, AA046490, AW674626, BF038335, BE741309, AA622857, BE514642, AI758646, AI568530, BE899462, BE314645, AA640935, BG260354, W16885, BE729175, BE834100, BE728332, AW674570, BE390209, AA323573, AW583200, BE276360, BE788833, BE734080, BG116454, BE378551, BF314517, BE394893, BE615490, BE277837, BE893234, AA035409, AA046762, AL536597, AA533663, BF830427, BE733877, BE618501, AW583301, BF344149, AI242340, BF854794, Z99383, BE298939, BE894136, BE548866, BF872337, AI564895, AI244738, F11543, BE958171, BE251364, AA081138, BE541241, BF700207, AU123424, AA524604, BE389991, BG033747, BF665573,

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42	HTSGQ95	144	1213625	AL536597, AW583200, AW583301, BG179799, BF667533, BF701034, AU155048, AU147529, AI243789, AI560241, AA224525, AI921744, AA640277, AA081138, AI583532, AU147226, BF915961, AI340151, AA601336, AA713769, AI207424, AU147352, AW518140, AA534064, AI216054, AA486829, AA676462, AW769687, AA487150, H68343, AA548029, AW833112, AW188427, BF826830, AU147078, AI889426, BF805601, AA177013, AV733378, AA551067, AL118925, N70044, AA158549, W96277, AA572983, AV732497, AI801505, AI356440, AA584862, AI800426, BF991881, BF991882, AW082076, AA468997, BF725844, AU145155, AA664126, AA491960, AA444166, AA525331, AW876459, AW973541, AI049504, AW013787; AI858691, AI709211, BE005805, H93717, AA666048, BF725884, AW876458, BE245594, AV762783, AA829044, AA601326, AW962006, AI797998, AA609826, AW662590, AW662588, AA652064, AW512300, AA618412, AL079894, T49451, AW504011, AV691908, AA610255, BF883766, AV696428, AW502796, AA601674, AW673267, AI355986, BE005811, AA648957, AI800706, BE501670, AV763135, AI917132, AA468494, AI434037, AI805699, AW104163, AW238341, AA284247, F16848, AA584769, H54252, AF092453, AC004253, AC008649, AC005695, AC020908, AL050349, AL049643, AC004841, AC005527, AC010789, AC004166, AP000501, AL035400, AC004972, AP001714, Z99716, AC005821, AC004089, AC005098, AC005209, AL023807, Z86090, AC027319, AL137129, AC002425, AC011455, AC005522, AC005206, AL031293, AC011469, AC005338, AL160175, AL022324, AC005971, AL022330, AP001727, AC005015, AC006312, AC005667, AL135927, AC020552, AC008745, AC005005, AC004659, AL034380, AC002554, AC008521, AJ277546, AL158830, AC002394, AC007225,

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42	HTSGQ95	145	1226328	BF793601, BE264355, BF059168, AI798238, BF316651, AI263924, BF514502, AI708865, T10449, BF855767, AW452145, AI394699, BF026003, AA485047, N23079, BE017996, BF591469, AA034518, H53662, N69293, AA456812, AI086440, AI468360, N89689, AA626634, AW631193, AI874264, AI300856,

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43	HLSAI43	53	1243888	AI658929, AA622809, AC004847, AC003108, AC006241, AC003010, AC011444, AL163279, AC005015, AL158040, AC004953, AC005295, AL031407, AC011895, AL137073, AC008551, AL096791, AL034420, AC020908, AL353748, AC008372, AC008403, AC009123, AC005529, AC005328, AC006509, Z98200, AC007850, AC010203, AL161731, AC022517, AC005081, Z94056, AF006752, AC009244, AC002425, AP001710, AC004089, AL031053, AC005779, AC011811, AL390738, AL117348, AL445465, AL136418, AC011462, AL023575, AC005098, AL049539, AC002477, AC004491, AF053356, AL031284, AL161670, AC002303, AC022154, AC005072, AL121890, AC004922, AC020904, and AC004099.
43	HLSAI43	146	1213409	N55560, AI811076, AA658101, AC004084, AC005015, AC006241, AL162615, AL137073, AC007383, AC004847, AL049539, AL135749, Z98200, AC003950, AL117348, AC004967, AC011444, AP001759, AL136172, AL035413, AL049843, AC004032, AL031286, AC008738, AC004551, AC008521, AC005071, AL031662, AL161670, AF053356, AL079335, AC007114, AL137796, AC005902, AP001725, and AC005624.
44	HNBTF02	54	1253163	AL525808, AL524460, AL525398, AL535552, AL524461, AL525846, AL535123, AL525223, BF663201, BF663208, BF969983, BE275108, BE275895, AV703489, AI151414, BF038378, BG166785, AI761082, N58441, BG149409, AI654101, AW339240, AA758040, AW440385, BE770847, AA677550, AA706893, BF508156, AW665376, BF530677, AI217787, AI658591, BF477855, AW152384, AI149742, BE669424, BE892709, BE349941, AA977493, AA536219, AW819586, AI376717, AW592564, AI005644,

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44	HNBTF02	147	1226356	AL525808, AL524460, AL535552, AL524461, AL525398, AL525846, AL535123, AL525223, BF969983, BF663201, BF663208, BE275108, BE275895, AV703489, BF038378, AI151414, BG166785, AI761082, N58441, BG149409, AI654101, AW339240, AA758040, AW440385, BF530677, BE770847, BF508156, AA677550, AA706893, AW665376, AI217787, AI658591, BF477855, AW152384, AI149742, AW964541, AA536219, BE669424, BE892709, BE349941, AA977493, AW592564, AW819586, AI376717, AI005644, BF593777, AA861871, AA536020, BF726489, AA884111, AI421262, BF059034, AI559673, AI052068, N51840, BE843155, AA865463, AW512183, AI984320, AA733139, AI884563, AI085891, AI271696, AI539839, AA479883, AI370924, AI095147, AI147781, AW965502, AA877448, AW819535, AW607532, AW152259, AA535765, BF854349, AW193317, AA996022, AI880144, AI800410, AW662846, BF223748, AV708490, AI767563, AA044645, AW958152, AI908462, AA588323, AA613303, AA938992, R53623, AA733206, AW571973,

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45	HNSCC06	55	1263307	BE409588, BE734445, BE901407, BF025948, BE614952, BE743554, AU125993, BE390314, BE256957, BE253147, BE258154, BE274147, AI192958, BE389838, BE537850, BE387783, BE390536, BE256422, BE258334, BE409102, BF795226, BE391787, BE543286, BE408304, BE733067, W39709, BE251706, BE292966, AW851119, BE278959, BE616308, W15487, AW939056, AA749428, BF795480, BE788770, AW977047, AI222705, R77439, BG117241, AI765573, BE279318, BF351247, AW880061, AL048927, BF351250, W52823, AA721368, AA804780, AA643419, AA179683, AK022749, AL078645, Z97985, AL109952, AL133275, AL121675, AC007955, U72787, AC006222, AC004621, AC011493, AC010422, AL035666, AL109801, AL117380, AC002350, AC004823, AL136305, AL096773, D42052, AL034376, AL359649, AL078639, and AL157361.
45	HNSCC06	148	1209025	BE734445, AU125993, BF795226, BE253147, BE258334, BE733067, BE256957, BE292966, BE278959, AW851119, BE616308, AW939056, BF795480, BE256422, BE788770, BE409102, BE251706, BE389838, BE390536, BE279318, BE743554, BF025948, BE390314, BE391787, BE409588, BE387783, BE258154, BE274147, AI765573, BE408304, BE901407, AL048927, BE614952, AK022749, AL109952, AL133275, and Z97985.
47	HCNCM78	57	1243864	AA553959, AW134688, AI831407, BE899580, AW516596, AW206923, AI948903, AI983767, AI339648, AI832391, AI833297, AA587764, BF001316, AI283185, AI304380, AI813445, AA857922, AI336470, AA938765, AI832498, AW970357, AI833021, AI285352, AW854263, AW970275, AI744428, AI336626, AW591238, AI732376, AI732377, AA534511, AI864896, AA422086, AW361498, AW361500, AW361502, AI766378, AA422178, AI833288, AI246768, AW351854, BF478262, AA535314, AW361503, AA283751, AW351839, AI720988, T25111, AX027767, AX027773, and AK025416.
47	HCNCM78	150	1225879	AA553959, BE899580, AW516596, AI948903, AI983767, AI831407, AI832391, AI833297, AW134688, AA587764, BF001316, AI304380, AI283185, AI813445, AA857922, AI336470, AA938765, AI832498, AW970357, AI339648, AI833021, AW206923, AW854263, AI285352, AW970275, AI744428, AI336626, AW591238, AI732376, AI732377, AA534511, AI864896,

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47	HCNCM78	151	1225880	BE899580, AW134688, AA422178, AW854263, AA553959, AI831407, AW516596, AI304380, AI983767, BF001316, AI948903, AI832391, AW206923, AI833297, AI339648, AA587764, AI283185, AI813445, AI832498, AA857922, AI336470, AA938765, AW970357, AW361498, AW361500, AI833021, AI285352, AW361502, AW970275, AI744428, AI336626, AW591238, AI732376, AI732377, AA534511, AI864896, AA422086, AW351839, AI766378, AA283751, AI833288, AI246768, AW351854, BF478262, AW361503, AA535314, AI720988, T25111, AL042488, AL046356, AL045891, AL043321, AI432666, AL041862, AL040207, AI432644, AL043089, AL042787, AW877209, AI431307, AI538850, AL135012, AL047675, AI431316, AI690946, BG252929, BE897632, AW858522, BE885490, AI539781, AI866786, AI494201, AW151136, AI539771, AI537677, AI500659, AI815232, AI801325, AI500523, AI889147, AI582932, AI284517, AI923989, AI500706, AI445237, AI491776, AW151138, AI521560, AI889189, AI500662, AI284509, AI889168, AI866573, AL042515, AI633493, AI866465, AI434256, AI805769, AI888661, AI284513, AI888118, AI872423, AI440252, AW172723, AI440263, AL042898, AI866469, AI434242, AI436429, AI859991, AI355779, AI371228, AI610557, AI860003, AI242736, AI887499, BE886728, AL042853, AI890907, AI433157, AI432656, BG029667, AL042655, AI521596, AL047163, AL047092, AL047611, AL043091, AL042729, BG110517, AL515375, AI559957, AI828574, BG257535, AI866510, BG251257, BF795712, AI371251, AI539800, AI539260, AI923046, AL042744, AI581033, AI538885, AI431238, AL045620, AI500714, AI491710, AI521571, AI648567, AL042365, AI539707, BG113712, BF727352, AI355008, BF968504, AI887775, AI590043, BF797072, BF338002, BE883591, AL042508, BG180295, BG181066, BG259587, AL042802, BG179586, BG111590, BF968622, BG114012, AI431321, BG260287, BG165260, BE895801, AI275175, BG164752, BG033403, BG034554, BG029194, BF983875, BG180046, BF528717, AW089557, AI366900, BG024457, AL045500, AI432653, BG261116, AI623302, AW197139, BF968984, BG178146, AL042551, BF347093, BG257383, AL042533, BG030750, BG181100, BG116926, BG166490, BG122277, AI499463, AL046990, AI610362, AL515373, AI440239, AV739574, AI537273,

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48	HCOKD57	58	1271607	AL514084, BF980786, BF000075, AI796517, AW070690, BG116779, AV729125, AL040719, BE905371, BF435812, AV758811, BF445032, BF038933, AU139160, BE817698, BE817689, BE817692, BF970673, BE817688, BE817690, BF980976, BE817683, BE219133, AW576078, AI492014, BF695375, AW341259, AW137190, BE739011, AA770505, BF436062, AW044212, BE829282, BE817686, BE930822, AW015617, BE905281, BE817687, AA460440, AV746720, AW515269, BE829316, BE770749, BF331445, BF667893, AI700452, BE817622, BF197030, AW050703, AI907066, N67813, BE829313, BE817504, BE167598, BG249234, BE167595, BF512427, AA720628, H27396, AW293068, AI458960, BE817627, H99488, BF983519, AW237464, AW516111, BE172367, BE817507, BE817447, BE817445, BE817440, AV748223, BF692864, BE872440, AV749079, AA573324, BE817623, BF329441, AA361602, BF329419, AA299162, BE770731, AW583451, BF329407, N56603, AI474862, BE817439, AA384824, D31551, BF342070, BF814761, BG166654, BE538997, AI469516, BF924856, BG255903, BF811808, AI445620, BF032768, BF726183, AI927233, BE967219, BF751997, AW827144, AV727264, AW160363, BF921291, AL079741, AI523806, AF263279, E07890, D14043, AJ238574, AF106518, AB028895, AB014464, AL117583, AF130099, AF130104, AL162085, AF217987, AX019230, I89947, AL110280, AF116631, I33392, AK026452, AX019229, AK026600, Y10080, X82434, AF112208, U35846, I48978, AK024992, AL137478, AL359596, AF177401, AF227198, AL133112, Y16645, AL133080, AL133067, AJ000937, A08913, AL050092, AL117432, AR038854, AK000137, U96683, A12297, A08910, A08909, AK026057, AL117626, AF118090, AF130077, AL389935, AL133560, AL359600, AL137459, AK027164, AL117460, A08916, A08912, AL050108, AB034701, A08911, A58524, A58523, AL389939, AF111112, Y10655, AF119875, AK026480, AL353957, A93350, AX010492, AK024533, AJ238278, AB050431, AK024855, L31396, L31397, S76508, A08908, AK026583, AL390154, AK000083, AF125948, AL133606, AK026647, AK026624, AF090900, I89931, AL122049, AL137526, AB048913, AL050146, AX006092, AK025465, E01614,

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49	HRAEO74	59	1209635	AW857559, AW860551, AI697075, and AK026923.
50	HTACM88	60	1253076	AI288755, AI828190, AI991170, AL525210, AA401831, AI820010, BG236281, AW080971, AA436421, AI183760, AA436436, AA427933, AA454879, AA929056, AI291005, AI709125, AI143034, BF736997, AW181949, AA887997, AI087367, AW392589, W49706, AV649907, AA613359, AI343895, AA564472, AI167351, AI128933, BG178655, BE876180, AA994804, BF743783, AI751316, AW130234, AA643538, AA481379, AW351505, R38636, AW004764, W48634, AA962531, AW203997, W49705, W48837, AA455222, BF375473, AA740790, AV736280, BE813536, AI572675, C06035, AA443505, AA911262, BE348886, AA962734, AV740202, AA291454, AA379425, BE812218, BE812373, AA379455, D20213, AI476379,

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50	HTACM88	153	1213431	AA621838, AI354847, BF768331, AA370455, AA773302, BE222564, AV731189, AU119532, BE740358, BE160473, AU117926, H12383, BF764092, BE731600, AV714931, BE867712, BE538259, BE541237, BG260565, AI537772, AA570230, AW405593, AV763305, AA594043, BF106319, AW817889, BF832641, AU144517, AV660988, BF792316, AI311234, AA605272, AC006953, AL137145, AC008041, AC009509, AC005546, AL445532, AC008958, AC004887, AL031390, Z97054, AC004166, AC005920, AP001437, AC005080, AC007707, AP000152, AP000011, AC007216, AC010598, AF030453, AC005088, AC009247, AL021546, Z98750, AC005520, AC008651, AC011455, AC006544, AC008753, AC006120, AC005031, AC008055, AL163249, AC004686, AL133215, AL358777, AC005821, AC002563, AC010422, AC007957, AC003104, AL031228, AP000208, AP001728, AL121933, AC006543, AL031311, AP001714, U80017, AL390039, AC068499, AC012384, AC004590, AC004655, AC073148, AC027319, AL035684, AP001710, AC078899, AC005391, AP000512, AC005919, AL022476, AC007050, AC009312, AC005669, AC005940, AC004965, AJ229041, AC004126, AC005668, AC011510, AL139286, AP001711, AC006483, AC002126, AL356422, AL445215, AL080243, AF070718, AC007597, AL163280, AL133232, AC025593, AC005098, AL355392, AC005522, AL354864, U85195, AL031005, AP000247, Z97056, Z95152, AC005839, AC002080, AF196779, AC009506, AL109897, AL031295, AE000658, AC004878, AB003151, AL049779, AL138717, AL050349, AC006505, Z93023, AC011445, AC006329, Z84469, Z98884, Z83840, AC007240, AC004079, AC010206, AC006581, AC008119, AC007052, AF169120, AP000133, AP000211, AC006312, AL136529, AL008726, AC006013, AC005000, AL136139, AC007201, AL121601, AL031681, AL132777, AC011442, AC008012, AC022148, AC002480, AL109976, AC008403, AC022816, AC011444, AC007225, AC010150, AC007881, AL109654, AC007731, AC008969, AC011811, AC002565, AP000355, AL022326, AC005921, AC007298, AP001716, AC005808, AC006451, AL034420, AB015355, AC006948, AC007880, AC021999, AC006597, AC005071, AL022163,

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50	HTACM88	154	1228352	AI288755, AI828190, AI991170, AA401831, AI820010, AL525210, BG236281, AA436421, AI183760, AW080971, AA436436, AA929056, AA613359, AA454879, AA427933, AI291005, AI709125, AI128933, W49706, AA564472, AA994804, AI143034, AW181949, AA887997, AI087367, BF736997, AV649907, AI343895, AW392589, BG178655, AA643538, AI167351, AI751316, BF743783, R38636, AW130234, BE876180, W48634, AA481379, W49705, AW203997, AA962531, W48837, AW351505, AV736280, AA455222, AA740790, AW004764, BF375473, BE813536, AA911262, C06035, AI572675, AA962734, AV740202, BE348886, AA443505, AI476379, D20213, AI288154, AA379425, F11072, BE812373, AA379455, AA291454, F01677, BE812218, T29574, AI640860, AI924885, AI940499, AA373077, W19208, AA632207, AA481366, AI249275, AI570820, AI167352, BE813549, AW994048, AW363436, BF245165, BE812378, AW136371, BF433323, AW604072, AI640645, AI738692, BG231592, AW949939, AI128941, AW338725, BE707831, BE881636, AA148025, AI471385, AI801128, AI478377, AW363441, BF767408, AV654244, M83246, A18757, I08456, AC006953, X51675, U08839, U09937, I08455, AF302071, AF302073, AF302072, AF230359, AF257789, AF302074, U09936, X74039, I08454, and U09346.
51	HBWBI44	61	1277904	AI279064, BF808316, BE502286, BG035106, AL525085, AI002918, AI655677, AI979295, AI954725, and AI335935.
51	HBWBI44	155	1159379	AI279064, AI002918, AI658541, AA465689, AP001207, AC012442, AC004084, AC011811, AC005940, AC004166, AL121895, AL136097, AC009244, AC005098, AC002544, AL022320, AC005622, AL356299, AC006597, AL121896,

				AL022318, AC004671, AC008750, AC004773, and AC005088.
52	HAGIF61	62	1243855	BE615911, AW024250, AA581416, AI798859, AI672399, AI830617, BE219023, AW024261, AI634552, AI678830, AA581434, BE675723, AI475894, AA836318, AI910508, BG149711, AI863379, AI357862, AI684341, AI687339, BF739932, BE466788, AW470389, AW662349, AW771538, W73842, AI859548, AI083937, AA614816, W69198, AI206255, W58108, BE502786, AA724515, BG168364, H97677, W69302, AI358221, AI830503, AI540802, AV714000, W58218, BF062532, AW192131, BE048082, BF528443, AA224329, H43162, T48025, AI380494, BG055888, AI380493, W69716, T23426, T23472, AA330730, AI586967, AA563998, F24016, AI689522, BF903224, AA788627, AI524127, AA917403, C02041, BE073275, AA308402, AW627500, BF738768, BF528665, AA890558, AA304909, H43098, W73698, AL390127, and AC025614.
52	HAGIF61	156	1212943	BE615911, BF348047, BF528443, BG168364, BF797908, BF528665, AV714000, AW850752, AW850753, BF311989, BF314844, AW024250, AI672399, AA581416, AI798859, BE219023, AI830617, AW024261, AI634552, AI678830, BE675723, BF206966, BE048082, BF062532, AI475894, AA581434, AA836318, AI910508, BG149711, AI863379, AI357862, AI684341, AI687339, BF739932, BE466788, AW470389, AW662349, AW771538, AI206255, W73842, AI830503, AI083937, AI859548, AA614816, W69198, BE502786, AA724515, H97677, AI358221, W69302, W58108, AA308402, BF903224, AI540802, AW192131, AA304909, W58218, W69716, AA224329, BF346644, H43162, AI380494, BG055888, AI380493, AA351550, BF738768, T48025, T23426, T23472, AA330730, AI586967, AW747892, AA563998, F24016, BF349796, AI689522, AA224075, AA788627, AI524127, AA917403, C02041, BE313633, BE073275, AW627500, AA223797, BF903213, AA890558, T48069, H43098, BF738021, W73698, AW956295, AW964422, AV658863, AW959868, AV692345, AV659536, AV706827, AV708704, AV704771, AV703819, AV727015, AV706342, AW964369, AW957428, AL390127, and AC025614.
53	HSYHD12	63	1280343	AL520080, AL532356, AL520079, AL527585, AL527586, AL526894, AV684581, AL526753, BE543419, AA233105, AI061464, AW000960, AA182932, W01643, N45263, N39195, AI700982, AA181583, AI493417, AA626568, AI735156, AI470553, AA704923, AI342329, AI763138, AA621175, AI382784, BE008953, AA977119, N71629, AW196544, BE778807, AV748461, AV682395, AW051088, BG166654, AI620302,

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53	HSYHD12	157	1209769	AL520080, AL532356, AL520079, AL526894, AL527586, AL527585, AV684581, AL526753, BE543419, AI061464, AW000960, N39195, AA233105, AA181583, AI493417, AI735156, AI763138, AI470553, AA704923, AI342329, AA182932, AA621175, W01643, N45263, AA977119, N71629, AI700982, AA626568, AI382784, AW196544, BE008953, BE778807, AV682395, AJ404004, and Z59762.
54	HTAGF12	64	1276746	AW467888, AW804959, AC006014, U52112, AC005098, AC004084, AC005488, AC004166, AC006241, AC004841, AC002067, AC003108, AC007546, AC020904, AC005899, AC004965, AC005052, AL135927, AC007227, AL033529, Z85996, AP001670, AC004531, AC004971, AC002365, AC005529, AC011462, AC007345, AC008569, AC004491, AL031276, AL035659, AC011491, AC011445, U52111, AC005332, AC008738, AL050335, AC006337, AC004000, U91321, AC007151, AF003626, AL035704, AC004106, AL163280, AC007182, AL096701, AL136136, AF053356, AC005482, AC004685, AL138878, AL157938, AL049569, AP000555, Z83844, AC025594, Z96074, AC006538, AC005102, U95740, AC007679, AP001718, AL118505, AC005839, AC006088, AC020908, AC008267, AC005740, Z84469, AL035685, AC004526, AC003101, AC003010, AC004967, AC004382, AC020906, AC006038, AC005088, AL121652, AL109627, AC007371, AC004980, AC008085, AC019221, Z93015, AL035413, AC004032, AL161445, AC020934, AL135901, Z98051, and AC009155.
54	HTAGF12	159	1222309	AW849533, AV718633, AV718938, AV699669, AW378532, AW949498, AV718908, AW950117, AV700313, AW129038, AV719049, BE069013, AA224902, AA568204, AA570740, AA483606, AW301736, AU148206, AI697239, AI697242, BG222214, BG230549, AA425924, AV764001, AW513905, AW467497, AA481887, AA302661, AA523695, H73550, AV716708, AA127570, AI418661, AA581247, AA837000, AA934680, AI432298, BG230529, AI567391, H53284, AA297006, BF920612, AI367551, AW069227, AI243789, BE178489, AA165505, D34614, I34294, AL157776, AC002550, AC004263, AP000313, AC005777, AP001718, AC006123, AP000050, Z85987, AL080243, AP000117, AC006966, AL352976, AL137059, AC009003, AL035587, AC007308, AC008687, AC004491, AC008569, AC005206, AC011462, AP000322, AC005829, AC006080, AC005236, AL034394, Z93015, AL109797, AC004084, AC005522, AL109743, AC005004, AC005667, AL096840, AL158830, AC005488, AC008764, AC005015, AC006115, AL353777, AL031311, AL049840, AC002477, AL390374, AC005005, Z84466,

				U80017, AL049709, AC010412, AC010789, AL137853, AC016396, AC011495, AC007917, AC006006, AF317635, AL035455, AK024205, AC020908, AL359204, Z83856, AC004953, AP000688, AL031432, AC016025, AF111168, AL121585, AF240626, AC008770, AL354836, AP001728, AP000053, AP000121, AC008040, AC005480, AL049779, AP001727, AL031602, AC020913, AL121891, AL355305, AL132777, AC010618, AF305057, AL096870, AC004980, AC010605, AC013734, AC009516, AC007383, AC007225, AL121997, AC007686, AL353807, AL117652, Z94044, AL049539, AC004019, AL355916, AC007263, AL139099, AL136300, AC005778, AC018673, Z98742, AP001724, AP001725, AL135928, AC007666, AL022323, AC004867, AC004526, AC009155, AC005839, AL121900, AC010526, AL031681, AL050318, AP000552, AC009244, AC011811, AP000503, AL079342, AC007597, AC004655, AC013429, AP000555, AC018663, AL050307, AC005391, AC006449, AC006480, AL031005, AC007766, AC007684, AL121915, AC005874, AF134471, AC005328, AC008537, Z95152, AL118501, AC006261, AL031133, AL031291, AC005280, L78810, AC009509, AC005747, AC005104, AC005207, AP000501, AC004257, AC005052, AL133387, AC005509, AJ004799, AC006511, AL049576, AL139384, AL136418, AL034405, AC002350, AC009756, AC003982, AC006126, AC009079, AC008009, AC024075, AL118520, AC010553, AC005215, AC005324, Z81364, AC008543, AC002301, AP000152, Z82190, AC011455, AC008762, AP001053, AC022149, AL157938, AC004000, AL354696, AC005225, AC003029, AL121653, AL009181, AC005914, AL133448, AC004962, AL031587, AB014588, AL137139, AL132653, S42655, AL132713, AC002390, AC087084, AL049766, AC010203, AL132795, AF134726, AC004659, AC006285, AL135839, AL353802, AC008474, AC005180, AC004477, AL138756, AC009247, AL137100, AP000300, Z93023, AP000565, AL049537, AL161670, AP000311, AC004166, AC007283, and AP001412.
55	HTHCA16	65	1243880	BE561009, BE561108, BE271257, BE560999, BE559581, BE560020, BE514226, BE560473, BE561815, BE396998, BE559603, BE560070, BE267963, BF974539, BE560782, BE396671, BE513801, BE268138, BE268135, BE296340, BE270072, BE269495, BE271160, BE513296, BE269405, BE561821, BE513289, BE513449, BE397933, BE397346, AW328031, BE267916, BE267977, BE270500, AW732742, AL041617, BE300743, AI004179, AW733048, BE300926, BE207729, AA977079, AI638067, AI810553, AL043588, AL040746, AI568276, BE740313,

				AI492067, BF527899, AA017019, AA973063, BE268669, AW577554, Z44581, BE207735, BG122414, BE839851, BE839956, BF975663, BE839944, BE839806, BE839820, AI990791, BE839892, BE839810, BE839906, BE839855, BF527373, BE839904, BE839896, BE839893, BE839895, BF931640, AV683249, AA357141, BE839822, N58603, BE839959, AI792408, AI791923, BE839888, BE839808, BE839889, BF155299, AW374023, W07130, BE839854, BF772089, BE839899, BE839960, BF879354, BF764629, AV647162, AV646714, BE839819, BE839961, BE839907, BE839898, BE839813, BE839962, BE839903, BE839801, BE839900, BE836824, AA506752, AC005071, and AF217981.
55	HTHCA16	160	1059497	BE561009, BE271257, BE561108, BE560999, BE559581, BE560020, BE560473, BE514226, BE561815, BE560782, BE396998, BE559603, BE560070, BE267963, BF974539, BE396671, BE268135, BE513801, BE296340, BE268138, BE270072, BE269405, BE269495, BE271160, BE397933, BE513296, BE561821, BE513289, BE513449, BE397346, AW328031, BE267977, BE267916, BE270500, AW732742, BE300743, AL041617, AW733048, AI004179, BE300926, BE207729, AA977079, AI638067, AL043588, AI810553, AL040746, AI568276, BF527899, BE740313, AI492067, AA017019, AA973063, BE268669, AW577554, Z44581, BE207735, BG122414, BE839851, BE839956, BE839944, BF975663, BE839806, BE839820, BE839892, BE839810, BE839906, BF527373, BE839904, BE839896, BE839893, BE839895, BE839855, AI990791, BF931640, AA357141, BE839959, AV683249, BE839822, N58603, BE839808, AI792408, AI791923, BE839888, BE839889, BF772089, BE839854, BF155299, AW374023, BE839899, BE839960, W07130, BE839819, BE839907, BE839961, BE839898, BE839813, BE839962, BE839903, BE839801, BE839900, BF879354, BF764629, AV647162, AV646714, BE839955, BE836824, AA506752, AC005071, and AF217981.
56	HNFIQ15,HWAAP41	66	1282887	AA833887, AW575462, AW510946, AI620223, AA648441, AW269713, AI524107, AA281769, AW304696, AI372986, BF115889, AI440497, AI826086, AI885846, AI148962, AI560987, AU154251, BE675218, BE207490, AW295615, BG235977, AW054789, AI554878, AI563935, AW439487, AI369278, AI609040, AI810003, AW965165, AI202784, AA720683, AI885219, AI871248, AA749067, AA280892, AI040456, W49531, AW006404, AI333761, AA045264, AA810174, AI033893, AA836425, AW316675, AI223206, AI817352, AA740402, AI151009, AW302593, AW469783, AA031829, AI807838,

				AA568174, AI921570, AA999995, AA602307, N94335, AI150388, BE883850, T23626, N81097, W37676, AA648458, AA935911, AA281428, AL537444, R50741, AI222836, AI285029, AA151329, AA626028, AA948149, AA853032, AA458986, AA807256, AL523211, AI015270, AI741627, AA621985, R79233, AI869588, R20646, AI986040, N99140, F37149, AL538472, AA045272, T58638, AW575463, AI368508, AI185496, AA769469, AA743471, AI560366, BF381797, AI741637, AW662063, AI738772, F28687, AA076441, AA127821, AI372985, AW796141, BF590617, AA627782, AA743487, AL522131, BG059881, BE902755, AA903626, BE902143, W23975, BG177827, AW084080, BF340302, BE790023, AA587120, AL047883, AA907245, BF892007, AL042954, AI952109, AI452772, BG255834, H41759, AA225339, AI174593, BF925363, AA830333, AV733470, AL040558, AV715462, BG107315, AA149526, AA764938, BG116399, AF001434, AY007161, AF099011, AF042856, AJ001388, AF140224, AB028456, AF130110, AF061943, AK026615, AF130105, AK025113, AK026973, AL109725, AF143723, L10376, X52128, AL096762, AL117460, E15324, AJ010277, AL133047, AK025356, AC020647, AR022283, AF130357, AL137658, AF017437, X67813, AL133565, AL137548, AF114168, X96540, AK027260, and AL356800.
56	HNFIQ15,HWAAP41	162	1201579	AL537444, AL538472, AL523211, BE559851, AW965165, AI871248, AL522131, BF115889, BE397650, BF683712, AI826086, BG235977, AI524107, AW575462, AI810003, AI885219, AA045272, AA045264, BE675218, AW054789, AI560987, AA833887, AA280972, AI554878, AI148962, AI885846, AW510946, AI563935, AA720683, AI620223, AW439487, AI372986, AI369278, AI609040, AA031829, AW304696, AI440497, AU154251, AA151328, BE207490, AI202784, AW269713, W49531, AI040456, AI333761, AA280892, W49578, AA568174, AI222836, AW006404, AI151009, AI033893, AW316675, AA740402, AI807838, AW302593, AI285029, AA810174, AW295615, AI817352, BE883850, AA836425, AA648441, AA948149, AI223206, N94335, AA281769, AA602307, AA999995, AW469783, AA749067, T23626, AI921570, R79502, W37676, AI150388, AA648458, N81097, F37149, AA935911, AA281428, N99140, R50741, H75402, BG177827, W23975, AA298081, AA151329, AA626028, AA853032, AA458986, AA807256, AA076525, AL138204, R20646, R79233, R68182, AI015270, AI741627, F28687, AA621985, AI869588, AA298080, AA280662, AI986040, AA459124, T58638, AW575463, R50285, AI368508,

				AI185496, R50436, AA769469, AA298084, AA743471, AI560366, BE890128, BF381797, W37675, AI741637, AI372985, AW662063, BE140883, AA280125, AI738772, T80700, AA076441, BF374320, AW387036, AA127821, AW796141, AW387048, BF590617, BE297808, AA127869, AA627782, AA743487, BF345882, BG059881, BE902755, BE295926, AA354619, BE745320, AA903626, W46303, BE902143, AW387062, N99901, AA345169, BF346209, BE269911, AI568612, AW084080, BF340302, AW134682, BE790023, AA587120, AL047883, AW003337, AI684918, AW082395, AA907245, AW117367, AW118157, BF892007, AL042954, AI952109, AU158013, AI452772, BG255834, H41759, AA225339, AI174593, BF925363, AA830333, AV733470, AL040558, AF001434, AF099011, AY007161, AF086188, AF042856, AJ001388, AF140224, AB028456, AF130110, AF061943, AK026615, AC007465, AF130105, AK025113, AK026973, AL109725, AF143723, L10376, X52128, AL096762, AL117460, E15324, AJ010277, AL133047, AK025356, AC020647, AR022283, AL137658, AF017437, X67813, AL133565, AL137548, AF114168, X96540, AK027260, and AL356800.
56	HNFIQ15,HWAAP41	163	1049987	AW575462, AA833887, AW510946, AI620223, AW269713, AI524107, AW304696, W49531, AI372986, BF115889, AI871248, AI440497, AI826086, AI885846, AI885219, AI148962, AW295615, AI560987, BE675218, BE207490, AW965165, BG235977, AW054789, AI554878, AI563935, AW439487, AI369278, AI609040, AI810003, AA720683, AW006404, AU154251, AI202784, AA810174, AA280892, AA045264, AI040456, AA031829, AI333761, AI817352, AI033893, AA836425, AW316675, AI223206, AA740402, AA281769, AI151009, AW302593, AW469783, BE883850, AI807838, AA568174, N94335, AI921570, AA999995, AA602307, AA648441, AI150388, T23626, AA749067, AA648458, N81097, AL537444, R50741, AA935911, AA281428, W37676, R20646, AA807256, AA151329, AA626028, AI222836, AI285029, AA458986, AA948149, AA853032, AL523211, AI015270, AA621985, AA045272, AI869588, R79233, AI986040, N99140, F37149, AL538472, T58638, AW575463, AI368508, AI185496, AA769469, AA743471, AI560366, BF381797, AW662063, AI738772, F28687, AA076441, AA127821, AW796141, AI372985, BF590617, AL522131, AA627782, AA743487, BG059881, BE902755, AA903626, BG177827, BE902143, W23975, AF001434, AY007161, and AF099011.
57	HNHPS28	67	1243890	AW021917, AL120976, AA468322, AW500250, AW977540, BF899670, BF899672, BF899671,

				AA632845, BE019467, BG222166, AA904137, AI446474, AA482681, R92262, C14692, AI753365, AA657835, AW515437, AW969743, AI014920, AI623805, T52478, AI282531, BE294700, AA483606, BE813932, AI923052, AA570740, AA533176, AI581486, AI143051, AW078909, AI446071, AW851816, AU131834, BE150087, AA570344, AA568204, AW004884, BF679672, AA878140, AW861583, AA468966, BE739086, AI360558, AA614163, AI588837, AA188676, AA862243, AA493898, AI984168, AA070899, BF526831, AU118852, AA223174, AL118925, AW516304, AW962006, H91062, AU156393, AI679413, AI304929, AI312309, AW968339, R43807, BG057207, AF157065, AL391114, AL035659, U35114, AL049776, U95740, AC024584, AC009307, AC005261, AC008068, AC005180, AL031431, AC006501, AC009086, AC007193, Z70050, AL021937, AC001228, AC007404, AL031280, AC008567, Z69917, AC011473, AC004778, AL034405, AC020741, AC011479, AC000092, AC006480, AC010271, Z82181, AC005881, AC011495, AF254822, Z73986, AP001747, AC004526, AL137818, AC007676, AC005015, AL163279, AL365505, AC018758, AF243527, AL117382, AF217490, AC005726, AC007969, AC010311, AC012076, AC018764, AC005098, AL031432, AL050335, AC009298, AC006211, AL110115, AC007878, AC003037, AL096700, AC007666, U02570, AL158040, AC002039, AC008265, AC000070, AL359763, AL162458, AC004765, AL133418, AL135924, AL096800, AC004854, AC004382, AC010326, AC008784, AF165926, AX039602, AC002484, AC011464, AC083871, AC010203, AC008626, AC007226, Z93015, AL135787, AC002470, AC008760, AC015651, AC005730, AC004448, AL354864, AC083863, AC007055, AC005080, AP001626, AC009087, AC002544, AP001685, AC005971, AL034379, AL022163, AC004089, AC008379, AC007308, AC008521, AL445466, AC006468, AL121891, AL136137, AC007684, AL121895, AL031311, AC007565, AF220542, AC006023, AL163853, AC010422, AL117348, U91326, AF015722, AC004805, AC008752, AL359457, AL121658, AC002543, AC011451, AC007900, AC009194, Z93930, AL139353, AL049758, AP000509, AF111168, AC027644, AC006275, AC005914, AC010200, AC008733, AF275948, AL020993, AC008649, AL031005, AC010102, AC008812, AL162390, AL353748, Z99570, AL035460, AL031255, AL034372, AC019227, AC002045, AC004583, AC005358, AC005736, D14872, AC000026, AF190465, AF207550, AP000959, AL157768, AC024952, AC007387, AC008560, AL034423, AC005324, AC010305, AC008764,

				AL163268, AC008745, AC009331, AC005288, AL031680, AL133391, AC004983, Z98742, AC008126, AC006543, Z98750, AL138976, AC002456, AC008616, AL109627, AP000099, AL137139, AL034555, AL078646, AL139421, AD001527, AC007860, AC005839, AP001745, AL035071, AC005522, AC020916, Z82180, AC005354, AC006334, AC008536, AL035587, AC008551, AC007312, Y18000, Z99755, AC008482, AP001435, AC005702, AC006544, AL133174, AC002472, AC006057, AC005406, AP000557, AL049745, AF001550, AL121886, AC004811, AC011470, AP000036, AC005911, AF073519, AC005037, AC006162, AC003002, AL161665, AP000514, AL137162, AP000008, Z99716, AC004980, AL078584, AL109952, AL138878, AC005280, AC007785, AL135905, AC007564, AL133245, AL137191, AC007907, and AC027319.
57	HNHPS28	164	1209276	BE813932, BE893349, AI807253, and BF950717.
58	HNTDN59	68	1280527	AW955777, AU127795, AV699578, BE621969, AI281940, AI346748, AU129292, BE005208, AA524503, AW449058, AI634820, BF514115, AA916758, BF000038, AU151450, BE467769, BE464881, AI523530, AW511445, AI862532, AA608828, AI949670, AW970765, AI857780, AW295536, BF571416, AI377542, AI093088, AI151251, AW614038, AV699485, AA287191, AA287100, AW770401, AA448285, BF737449, AA878147, AW337811, AI094118, AW593438, AI679170, AA126509, AA824653, AI335819, W17300, AI926067, AA724997, N89777, BF445215, AI376326, AA693394, BF898929, BF330087, H24089, W20017, AA780601, AI262511, AA651916, H95444, AW023522, AA708871, AW630974, AW605999, BF968034, H95445, R43926, AW380437, C03566, AW452210, R18816, H22911, AA334867, N91375, R84237, AW020824, BE071575, W24107, D62482, N91929, AI859420, D62471, BF946583, BE708592, BF195756, AA658355, AI962246, AA282731, BE967075, AW167926, AK023008, AK022861, and AL163853.
58	HNTDN59	165	1215793	AW955777, AU127795, AV699578, BE621969, AI346748, AI281940, AU129292, BE005208, AA524503, AI634820, AA916758, AU151450, BE467769, AI523530, BE464881, AW511445, AW449058, AI862532, BF000038, AW970765, AA608828, AI857780, AI949670, BF514115, BF571416, AI093088, AW295536, AI377542, AI151251, AW614038, AA448285, AW770401, AA287191, AV699485, BF737449, AA287100, AA878147, AW337811, AW593438, AI679170, AI335819, AA824653, AI094118, AA126509, AA282731, W17300, AA724997, AI926067, N89777, BF445215, AA693394, AI376326, BF898929, H24089, AA780601, BF330087,

				W20017, AI262511, H95444, AW023522, AA708871, AW630974, AW605999, H95445, AW380437, AA651916, BF968034, R43926, C03566, AW452210, R18816, H22911, AA334867, N91375, R84237, W24107, AW020824, BE071575, D62482, N91929, AI859420, D62471, BF946583, BE708592, BF195756, AA658355, AI962246, BE967075, AK023008, AK022861, and AL163853.
58	HNTDN59	166	1215794	AI859420, BF330087, and AL163853.
58	HNTDN59	167	1210379	AL529061, AL529060, BF025889, AI185800, BF570353, BG035690, BF570347, BF972830, BE797551, BE621696, AI815914, BE733418, BF568490, AI355060, BF663029, BF568811, BE531071, BF238101, BF972804, BE615211, AI720942, BE562996, BF569853, BE727514, AI401205, AI041996, BF686541, BE614837, BE910466, BE744909, BF686056, AI992188, BF568527, AW080259, BG255729, BF795533, BF972645, BF569845, BF027352, BE728209, BF975164, BE615946, AW080260, BE612647, BE874826, AI478699, BE730928, BE741590, BE616224, BG033808, AV704355, BE537861, AW162630, BE394173, BE868076, BE906924, AI749777, BG177826, AI832416, BE378109, BE781845, BF684059, BE314958, AI949614, AI565597, BE736455, BE871915, AI859275, BE384814, AW051807, BE294364, BF972262, BE893828, AI624559, BE745624, BG056658, AV702685, BE889557, AI811664, AW262649, BF238268, AW150095, BF970880, BG120687, AV714903, AA654454, AA552688, AW304868, AW102953, AI570837, BF127636, BE858287, BE548275, BE873943, BG259729, AI921295, BE874247, BF568476, BF125599, BF027446, BE884117, BE621459, BE019587, AI660088, AW769076, AI589608, BG056650, BE906768, BF127827, AW327521, AI814476, AW327501, AA644002, AI138313, AW072677, AI970696, AI188158, AI422165, BE389121, AA732365, AI092848, AI143551, AA743939, BG059883, AA774241, AI633416, AW327574, AI419462, AI149132, AI038173, AA417137, BG030545, AI097634, AA989522, AA628121, AI017702, AI339841, BF569101, AA770673, AA747736, AI002563, AI142066, AA451650, AI094916, AA576291, AI025480, AA191340, AA526372, AA845860, BE906357, AI423595, AI131527, BE770914, AW161032, AI609048, AI933016, AW827283, AI819166, AI025652, AI073352, AI055858, BF760056, BE733802, AI309777, AA688407, AI079826, AA813021, W57669, AW068728, AI359878, AA316104, AV645712, AI762655, AA766876, T67923, AA191119, AA442295, AI309331, AA307611, BF354705, BE884749, AW572477, AW884641, AW161064, AW089981, BE315556, BE870709, AA281383,

				BF035335, AV655428, BF797165, AA527519, AW068469, AW002793, AI271805, AI300885, AA715400, AA410906, AW801345, BE256030, AW020972, F27646, H28271, AA834150, H39530, H25212, AA602160, AA229017, AV725738, N59365, BF033589, AA761426, AI815639, AA835946, H04530, AA148671, H42081, N36940, H45682, AA071439, AW592055, AI022860, AW605541, H42040, H19360, AA740357, H39988, BE163159, AA989516, AA923346, H24393, AA766621, AW769544, R73921, W81568, H45724, BF026382, AV646342, BF445725, AI758297, T96942, AI525255, AA978349, AA416983, AA460758, AA083783, W23113, R83209, BF760402, AA603765, D13900, X98129, X98127, X98128, X98126, T60246, T60128, T68071, R07754, R10635, R10636, T79112, T97051, R19583, R20438, R27986, R28244, R43558, R43558, H16202, H16203, H18921, H42233, H42306, H42686, H42732, H44551, H61138, N93540, W02759, W21348, W24769, W74207, W79721, W81615, AA055481, AA071211, AA148877, AA460159, AA229175, AA514605, AA534834, AA551880, F15667, AA658858, AA658940, AA661733, AA761406, AA872483, AA888651, AA654808, AA410750, AA450243, AA626255, AA813735, AI028772, AI091947, T11022, Z25184, D25834, F00278, AI245129, AI274610, AI469741, AI469793, AI420154, AI566809, AI191000, AI637590, AI263732, AI263765, AI524761, AI301254, AI336088, AI682747, AW008707, AW075313, AW518471, and AW779496.
59	HNTQM17	69	1283173	AI207452, AV710565, BF794024, AI949938, AI936201, AI829706, AI631489, AI094060, AI093751, AA913548, AI796021, AW054881, AI031866, BE084604, AW875236, AA962640, AI092761, AA005229, AI669801, AW204350, BF091658, AI608820, R56378, AA913113, AI470546, AI914019, AA706311, AI692760, AI024447, AI928379, AA483725, H05004, AW955704, AW953941, AA595634, R56278, AA364859, H05003, R83285, AW296235, AI369969, BG029062, BF931159, BF213510, AI991391, AI468617, AI767931, W19922, AW815774, H51728, AW967633, BG108591, AA251809, AX041040, AF119899, and AF153906.
59	HNTQM17	168	1209252	W19922, AW967633, BG108591, AA251809, R38139, AA431646, H58518, R77536, R62239, AA010808, T47540, and AX041040.
60	HNTTF76	70	1243907	AW151247, BE077105, AW272389, AW275432, AI791659, AI358928, AI984168, AI355246, F23338, BE154909, AI336771, BE328286, BE043339, AI288033, BF940118, AA298365, AW974363, D44672, BE073116, AI973173, AA489390, AA533040, BF528591, AI801563,

				AU120416, AA666295, BF221463, AI174703, AL035977, H79601, AI285651, AA493789, AI978712, AW510403, AA397355, BF678348, BE245594, AA810158, AA551968, AI283938, AA484892, AI123488, AA676592, BF681369, BG231195, AA503144, AV751848, AA729037, AW008184, AW166879, AI090377, AI678812, AI915081, AA595661, AU151751, AW069227, AW439867, AA846923, AL048060, AI797998, AW880986, AI816058, AA568314, AU160445, AW970588, H82636, AA573067, AI697235, AU159614, BG110480, AA492424, AA832145, AI792092, AW963397, AI821056, AI821805, AA838091, AA721506, AW341978, AI565084, AI249688, AI355103, BF668362, AI224619, BE042511, AI065031, AA535216, AI697239, AA525753, AI697242, AL023804, AC004106, AC004408, AC006241, AC009516, Z48051, AC006162, AC004025, AC026704, AL050328, AC004491, AL137012, AC002544, Z75407, AC006511, AL050349, AL139396, AL139100, AC006473, AL158823, AC002418, AC006210, AL353804, AL031662, AC011484, AL158830, AF134726, AC010150, AC008074, AC009244, AL121712, Z83843, AC010205, AC022148, AC004832, AC005409, AC004386, AC008752, AC016995, AC011470, AP000503, AC005911, AC005940, AC003029, AL049636, AC002314, AL117694, AC006312, U82828, AL109743, AC002425, AL008726, AL136137, AC006013, AC002404, AC004821, AC008738, Z83820, AC009032, AL136969, AC011465, AL158040, AL109797, AL133273, AC005695, AL158172, AC005531, AL133383, AK027128, AC004805, AL445490, AL031584, AC068499, AL049610, AL034420, AC008984, AC007226, AL035420, AC007785, AC005778, AC000039, AC002310, AC010084, AC007216, AL355520, AP000045, AC005052, AP001477, AL031297, AC007899, AP001712, AL139318, AC008762, AC005014, AC008521, AC005284, Z84480, AL023553, AL096791, AL034548, AC001642, AC002430, AL008725, Z98304, AC005736, AC004846, AC019181, AC006132, AC004797, AF015416, AC006441, AC005031, AC020728, Z97183, AL138836, AC020906, AL359846, AC005231, AL022323, AL136132, AL022320, AB003151, AC007563, AC007559, AC002073, AC004253, AL035681, AC009086, AF217413, Z83847, AC003101, AC009248, AL049795, AL159169, AC006468, AC002350, AC011299, AL121891, AC007182, AC005049, AC006023, AL109827, AP000501, AC006017, AC007384, Z82243, AC025436, AC005924, AC011475, AL009181, AC005593, AP000553, AL121829, AC002045, AC006121, AP000512, AL022316, AL136305, AL049872, AL096814, AL162740, AC012000,

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60	HNTTF76	169	1213468	AL023804.
61	HCFGD60	71	1253155	AW593931, AW663439, AI651376, AI218380, H23154, H09531, AC003093, AL137013, AL137918, and AL352979.
61	HCFGD60	170	1212775	AW593931, AW663439, AI651376, AI218380, H23154, H09531, AC003093, AL137013, AL137918, AL352979, and AC016995.
62	HMUEP30	72	1262057	BE729574, AL525054, BE734296, BE613340, BE745405, BE549234, BE311981, BE899322, AI079540, BE742508, BE379419, BE903604, BE612600, BE747302, BF339777, AW301090, BE877226, BG164618, BF033662, BE909447, BE782991, BF792659, BE788807, BE746235, BE259564, BF686415, BG116654, AW245743, AL110467, BE265746, BE382926, BG167167, BF316896, BE266690, AI870747, AI435074, AI810818, BG249818, AA426021, AA443445, AI675429, BE254649, AI380916, AW016054, BF939243, AW197499, AI968701, AW015418, AI085552, AI803701, AI609029, AI917395, AI627419, AI243526, BF448768, BF350582, AI813835, H68793, AW271667, BE780379, AI184105, AA418059, AA838309, N36450, AW245387, AA054185, N51652, H06674, AA852859, AA505926, W00635, AA428116, AA993193, AI350611, AI074877, T71376, AI813850, AI609552, H68794, BE829913, H82530, AA836943, AA852860, AA557951, BF928087, H86659, BE890771, AI499309, BF130572, BE840422, AI623897, R96119, AI867284, AW002546, AW630507, H96259, AA814467, AA443541, AA417955, T71246, AI288285, BF342070, AI500077, BF055737, AI611348, AL038445, AI917252, AL041772, BG250190, BG260037, BG109270, AI866770,

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				AF130105, AK026927, AF138861, AX006092, AK000323, AF026816, AF177401, AK025484, AK026647, AK026865, A03736, AF106862, AB052191, X82434, AF119894, Y16645, AL359618, AK026651, AF175983, AF017152, AK026532, AK000718, AL137527, U91329, AK000652, AL359941, AK027113, E03348, AF113689, AL133093, AF119875, AL389978, A65341, A77033, and A77035.
62	HMUEP30	171	1209865	BE903604, BE788807, BE379419, BG116654, BE782991, BE549234, BF686415, AL525054, BE909447, BE745405, BE382926, BE877226, BF792659, BE729574, BE734296, BG167167, BE746235, BE612600, BE266690, BF033662, BE742508, BG249818, AA443445, AI380916, BE747302, BE899322, BE254649, H68793, N36450, AA054185, H06674, BE780379, AA428116, BF316896, AA852859, T71376, BE829913, H82530, BE311981, H86659, BE259564, BF130572, BF339777, BE613340, BG164618, BF350582, AW630507, AW245743, BE890771, BE265746, AA443541, AA838309, AL110467, and AC011479.
63	HNSCA10	73	1268201	BG260541, AW967069, BE541744, BG028272, BE546267, BE561971, BF036322, BF064225, BF340450, BF245281, BF968759, BG027740, W56044, N35799, AA233837, AI276495, AA478375, BE074335, AI276218, BE539688, AA679425, AW300731, AA700229, AI986265, AI310474, N68373, AA351865, AA009569, C05871, AW137718, AA422073, AV658880, AA211039, AA317491, C06442, AI186371, AI468426, AA232803, AA541363, AW380398, H51981, W28357, AA478315, AA234338, AW079108, AW972914, AA234372, T98354, T98355, BE878609, AI383307, AA680060, AI932918, BF850967, AA441825, R06867, AI143413, BF734394, T81721, AI831550, AI857452, AI949949, AA295711, BF433630, C02103, BG151447, AI472405, BE551108, AV739493, AW999933, AA441888, AI952677, AK027031, AX041033, AC004050, and AL096861.
63	HNSCA10	172	1209403	BE541744, BE561971, BF968759, BE878609, BF850967, R06867, T81721, AI831550, AI857452, AI949949, AA295711, BF433630, BE551108, AV739493, AK027031, AX041033, and AC004050.
64	HTPAO67,HAPNY67,HAWCB75,HBMTN71,HE9GW86,HUVCQ29, HUVCV06,HWEAC51	74	1280558	AW888224, AU140905, BF526339, BF914797, AW391265, BF672993, AA196345, AW580939, AW511241, AA150505, AI937452, AV715700, AI693483, BF732946, AW270912, W72082, AI623367, AW792827, AA625461, AW070540, AA702989, BF693967, BE930195, AW005477, AA745718, AI341881, BF433329, AI081372, BE549661, BF114825, BF114817, BE825874, AU158733, AA491502, AI290320, AA196201,

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66	HSLFK66	76	1271609	D62414, AA181545, D79573, AA641508, AA669547, AA182437, D79561, T58386, D79571, D62426, and AA552375.
66	HSLFK66	176	1224406	AV761859, D79520, D62414, AA773146, AA570549, AA181545, D79573, AA182437, AA641508, AA962710, AA669547, AA307713, C16292, D79561, T58386, T51211, T53617, D79571, D79560, AA164697, D79576, T51316, D62426, AA164269, AA552375, and Z70707.
67	HCFPE46	77	1243901	BE906104, AA126510, BE676563, AA631935, AI083764, BE208817, AV655556, AA825589, AA404716, AI434722, AI144498, AA404589, AW978956, BF760247, AW835197, AW835198, BE269425, AI919158, AI656772, AI436732, AI932739, AI859648, AI524179, AW005157, AI631651, AI621039, AI561356, BE966927, AI961414, AI683555, AI433590, AI919500, AI973104, AI784214, AI453248, AI653664, BE965093, AI493567, AA761608, BE962390, AW131282, AI864836, AI828676, AA765198, AI553645, AW055252, AW072413, AA449768, AI680221, AI422050, AI763414, AC004643, AL442083, AF267849, Z97214, AK027095, I32738, U62966, AL080317, and A59621.
67	HCFPE46	177	1223989	BE906104, AA631935, AA126510, AV655556, BE676563, AI144498, BE208817, AI083764, AA404716, AI434722, AA825589, AA404589, BF760247, AW978956, AW835197, AW835198, BE269425, BF976690, BF313964, and AC004643.
68	HNGPB91	78	1253113	AI282479, AW514662, AA704009, N23096, AV691556, AV693536, AV697609, AI360558, AI821714, AI792133, AI791913, AA857812, AW105729, H73550, AI821785, AI224619, AA483606, AA602017, AA916430, AI267356, AA469230, AA570740, AL041706, AC007011, AL079342, AC005874, AF134471, AC018642, AP001711, AL022163, Z84480, AC010519, AC004865, AL161445, AL022315, AP000030, AC005544, AC003962, Z98949, AL008719, AC005527, AL050335, AC005529, AC020728, AC018719, AC005562, AL109935, AP001725, AC004659, AL136418, AL355499, AL022316, AC004971, AC002991, AP000251, AL022330, AL158823, AC018663, AC004253, AL035072, AC017100, AC009044, AC006974, AC008812, AC006515, AC004805, AP001729, AC004638, AC006241, AL136137, AL096701, AC004816, AC009783, AP000689, AC007055, AC010618, AC004032, AL121920, AL034429, AL049870,

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68	HNGPB91	179	1045322	AA744094, BE242452, AA225273, AW574958, AW572140, AA297670, AC008736, AC011475, AL022316, AC008521, AC007666, AC087095, AC016831, AC004491, AC025275, Z97054, AC004846, AC008812, AC007000, AL109935, AC020552, AL031662, AC004824, AC005041, AC013434, AC009948, AC006530, Z97630, AC005081, AC007707, AC005730, AL354720, AL158040, AP000036, Z99716, AL049776, AC006088, AC006023, AL049780, AC004821, AP000555, AL024498, AF190464, AC005291, AL080243, AL008723, AL049872, AL157372, AC004797, AC000353, AC007193, AC006285, AL121936, AP001717, AL049840, AC005899, AC078854, AC005231, AF195658, AC010326, AC005071, AL008718, AC005015, AC011442, AC022201, AC002425, AL035072, AC004975, AC011470, AL117336, AC007546, AL022315, AC020916, AC008641, AC002550, AL133215,

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69	HRADV31	79	1275159	BE616483, BE614781, BG167480, BE160498, BE160502, BE160500, N30135, BE160501, BE160497, AI767701, AI633623, AI140698, AW269969, N34283, AA610009, AA535713, AA904500, AA135305, AW043844, AW168046, AI271558, T65377, AA830555, AA779492, D29317, N51615, AW168340, R42844, AW149189, AA910171, AA679759, AI262864, H20852, AA096462, T77049, T51392, H22970, H08110, AA370573, AA136386, AW592312, F09407, R40094, T15987, T35272, AI470445, N72424, AA361165, H08109, BF840352, H20903, R21459, H22760, R14782, T65454, F11747, and AL117635.
69	HRADV31	180	1209606	BE160502, BE160498, BE160500, BE160501, BE160497, AA096462, T51392, AA370573, and N72424.
69	HRADV31	181	1046790	BG167480, BE616483, BE614781, N30135, AI767701, AI633623, AI140698, AW269969, N34283, AA610009, AA535713, T65377, AA904500, AA135305, AW043844, AI271558, AW168046, AA830555, AA779492, N51615, D29317, AW168340, R42844, AW149189, AA910171, AA679759, AI262864, H20852, T77049, H22970, H08110, AA136386, AW592312, F09407, R40094, T15987, T35272, AI470445, AA361165, H08109, H20903, R21459, H22760, R14782, T65454, F11747, and AL117635.
70	HNBVG70	80	1243889	BF341007, BF110353, AI498144, AI452515, AW269396, AW052151, AI418007, AI799477, AI689745, AI742906, AI624831, AI671017, BE220286, AW243321, AW269568, AW016809, AI819941, BE220815, BE328187, AI909029, AI910872, AI369619, AI214589, AI912142,

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70	HNBVG70	182	1225912	BF341007, AI498144, BF110353, AI452515, AW269396, AW052151, AI418007, AI799477, AI689745, AI742906, AI624831, AI671017, BE220286, AW243321, AW016809, AW269568, AI819941, BE220815, BE328187, AI910872, AI909029, AI214589, AI369619, AI912142, AW663724, AI796721, AI913870, AA936264, Z43546, AW882471, AW474263, T17017, T71999, AA988210, BE275875, AI655881, R07576, AI474210, T67045, AI383567, T08597, T65475, H42725, T65399, F13536, T87843, C20646, T67046, R07577, H42757, W27492, Z39615, F08143, AA718920, R45981, AW954424, H83823, AA377421, F11115, R46490, BF816811, AI340603, AW827206, AI284517, AA420722, AL036274, BE965758, BE964636, BE964876, BF914297, AA572758, BE909398, BE874133, AI537677, BE966011, AV710950, BE885490, AA259207, BE966787, BE887488, AI312152, AL119836, BF885675, BE886728, AI345735, AI312428, AW075084, AI950664, BF872670, AI349937, BE172767, AW089572, AI348897, AI307708, AI500659, AL036802, AI349598, AW068845, AI612885, AL514793, AI340627, AI445237, BE172412, AW151138, AW059713, BF344201, BF856052, BG114104, AA176980, AI918435, AL039086, BE965192, AI702073, BE963918, BE904051, BG252929, AI366549, AI636719, AI539153, BF818009, BE904178, BE964767, BF812961, BE894455, BE964614, BE964661, AI539771, AA974049, BF032768, AW403717, AW827289, BE895585, AL036396, AL042365, AI349933, BE877769, AL038605, AI866608, BE964700, AI340519, BF904194, BG178809, AI471909, BE875407, BF990167, BE047952, BE885048, BE881089, AI589993, BE965355, BE965556, AI753683, BF909758, AW806761, BF792378, AA804740, AI500523, BF812438, BF885000, BG113299, BE965432, BF766536, AI500706, AI754897, AI491776, BE965599, BF814412, AI349226, BF915536, BE965121, AI567612, AI633125, AI815232, BE965481, AI521560, H14460, AW813006, AA493647, AW673679, AI334884, BF343764, AI349957, AA579232, BF904177, AI801325, BF038131, AI500662, AI432570, AW020693, AW268253, AI862144, BF884999, AI349256, BE965307, BE011880, BG257535, BE963838, AW161579, BG105895, AI343059, AI433157, AI537837, AA136379, BE965621, BE621256,

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71	HCFGK19	81	1253156	AL041924, AV756491, BG029528, BF854308, BF854244, AF246229, AW504485, BF725844, AI085242, AV762633, BE062476, AI887235, BF678990, BF681619, AA760655, T74524, AV761107, AI272052, AW969667, BF946053, AV760019, BE674881, AV742175, AW500684, BF868994, AV682003, AI755214, BG115297, BE147075, AW468009, BF805088, AV759972, AI754567, AV758870, AW088846, AW963463, AI623720, AW023111, AA502532, AW969831, BF879045, AW402784, AW970940, AA515048, AL135357, AI733856, H07953, AW576251, AA833875, AA833896, AW872736, BE158716, AL042667, AL042670, AV760391, AW013790, AI310787, BF965290, AI609972, AI963720, AI859946, AW969743, AI282479, BF917346, AW270258, AV711465, AV763550, AW327624, AW328446, AV760389, AL138455, AA536040, U95743, AC005592, AR036572, U91328, AL035667, AF205588, AL136501, AC066585, AP001705, AC008569, AL034372, AL117337, AC002554, AC009530, AL161449, AC004824, AC005052, AL135783, AC011890, Z82194, AL137795, AC005874, AF134471, AC008134, AC016396, AC002492, AL138726, AL138478, AP001671, AC009087, AP001694, AL031311, AL096703, AC006211, AC005273, AF186190, AL031230, AC009405, AL109804, Z84483, AL353804, AC016751, AL133467, AL121890, AL132657, AL133376, AC008079, AL035555, AC009784, U95739, AP001748, AL034351, AP001688, AL135927, AC007227, AC003982, AC004466, AL138752, AP001631, AC034242, AL118501, AL096870, AL356057, AL121970, AC005534, AC005406, AP001713, AL022396, AC008249, AL133405, AL034371, AC008119, AL133372, AC004832, AL356010, AC007283, AC006390, AC068799, AC034194, AL121936, AL163246, AL121932, AC002394, AL023877, AC007226, AC010206, AC010598, AC006994, AL031229, AP001610, AC009247, AL163267, AL031658, AC018697, AC004166, AC005940,

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71	HCFGK19	183	1213458	AW839310.
72	HNGOG04	82	1243925	AC009492.
72	HNGOG04	184	1212831	AC009492.
73	HDCGC29	83	1253157	BG105848, BG035441, AL162212, and AC005081.
73	HDCGC29	185	1210197	BG030548, AI620284, BG163623, BG035441, BG034001, BG250790, BG122005, BG031205, BG178197, BG164994, BG105848, BG260144, BF971016, and AC005081.
74	HNGNT27	84	1261927	AW975169, AW245747, AL044340, AI537133, AI821467, BE063437, AW303196, AV682003, AW301350, AL037632, AI613389, AW020094, AW274349, AW021399, BF347791, BF347740, AI133029, AI719550, AI821596, T50676, BG029528, AA912287, AL046746, AV760019, AI334443, AA720774, AF001548, AC011540, AC004824, AC016995, U91323, AC008745, AL355392, AC008764, AL353807, AC018751, AC005261, AC011475, AC004659, AC006511,

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74	HNGNT27	186	1213013	AF001548.
75	HMUHD72	85	1281806	AL519919, AL523154, AL519918, BE734820, BE732499, BE734653, BE900311, AV757051, BG111889, BE298114, BF309539, BF797896, BE264515, BF310702, BE797906, BF345540, BF316978, BF309258, BE540917, BF668006, AI792617, BF182982, BF205381, BE278367, AI191836, BE245875, BE386622, AA135424,

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75	HMUHD72	187	1209710	AL519919, AL523154, BE734820, BE734653, BE732499, BE900311, BG111889, BE264515, BE298114, AV761083, BF309539, BF797896, AL535244, BF310702, BF345540, BE797906, BF316978, BF205381, BE278367, BF182982, BF309258, BE540917, AI792617, BF207185, BE386622, BE247361, BE247344, AI191836, R56363, AV652257, AA683257, T33685, BE246526, BF851311, N26459, BE246491, BE769477, T06623, AA305268, BE019484, BF850169, AA135245, AV652223, BE245574, D59427, BF847837, BF683313, AA137155, AL523153, BE246931, BF847823, AW964672, T35739, AA381753, AV649969, BF849496, BE245875, BF810571, BE242136, AA353958, BF346400, AA156166, AA181171, BF835889, BF058660, AA504226, BF209123, AA090078, AW292747, AA931847, AA496208, BF746750, AW884429, D50931, and AC005740.
76	HLYCK47	86	1272921	AI300176, BF339231, N32601, BF526118, AA894528, AI193100, AI749282, AI200645, AA917673, AA577400, AW001112, AI687717, AA703086, AI342526, AI561024, AI141075, AA922077, AW953836, AI274361, AI184968, AA922163, W92736, AI815092, BF821354, AI682589, AW000838, BF879161, BF878968, AI283829, AI346224, AI718510, BF821349, N38801, AA443822, AW966426, AA609464, AI285277, BG060138, AA827271, AI274203, AI278912, BF879241, AA485613, AI811138, AI291153, AI598054, AW515183, C17007, AA954441, BF525949, AI272748, T95291, AA508675, AW858976, AI582743, AI304507, BF343049, BF823040, BF342466, R71353, W92820, R47872, AI749077, AI523358, AA025765, R47871, AW953891, AI459266, AI352318, AW629891, H66689, R66274, AI873364, H78056, T27046, H90673, BF737942, AI336608, AV689909, H64116, T72087, T95371,

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76	HLYCK47	188	1221159	BF343049, BF525949, BF339231, BF342466, AI300176, AI193100, N32601, AW953836, AA894528, AA917673, BF526118, AI200645, AA577400, AW001112, AI687717, AI141075, AI342526, AI749282, AA922077, AA703086, AA922163, AI184968, W92736, BF821354, BF879161, AI274361, AW629891, BF878968, BG060138, AI682589, AI598054, AA443822, AW966426, AI346224, AI283829, AA827271, AI561024, AA609464, BF821349, BF879241, AI285277, C17007, AI523358, AI582743, AI274203, AI278912, AW000838, AW953891, AI811138, T95291, AA485613, AI815092, AA954441, AI718510, AI272748, BF823040, AI304507, N38801, AW858976, AI291153, H90673, W92820, R71353, R47872, AA508675, R47871, H64116, T27046, R66274, AI352318, AI749077, AV689909, AA025765, H78056, AW515183, AI873364, AA640081, H66699, H66689, R24350, H42114, T95371, BF737942, BF087543, T72087, AI459266, AA025953, AI336608, BF820542, AA383872, H64951, BG012708, D31533, R72785, H01871, BE769806, AI749260, H89819, H64952, BE769826, R72786, BF349116, R62666, AA368991, H01130, N45434, AA371827, AW374237, H73228, N90491, AA295668, N69227, BE140683, AW135690, AW374232, BF881707, AW610099, T16823,

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76	HLYCK47	189	1221167	BF343049, BF525949, AI300176, BF342466, BF526118, AW953836, N32601, AA894528, AI193100, AI749282, AA577400, AI200645, AA917673, AW001112, AA703086, AI687717, AI342526, AI561024, BF339231, AI141075, AA922077, AW629891, AI274361, AI184968, AA922163, BF821354, BF821349, W92736, AI815092, AI682589, AW000838, BF879161, BF878968, AI346224, AI718510, AI283829, N38801, AW966426, AA443822, AA609464, C17007, AI285277, BG060138, AA827271, AW953891, AI274203, AA485613, AI278912, BF879241, AI811138, AI291153, AI598054, AA954441, AW515183, AI272748, T95291, AI304507, AA508675, AW858976, AI582743, BF823040, R47871, R71353, AV689909, W92820, AA640081, R47872, AI749077, AI523358, AA025765, AI459266, T27046, AI352318, H66689, R66274, H78056, AI873364, H90673, H64116, H42114, AI336608, T95371, AA383872, R24350, AI749260, BF087543, T72087, AW029317, AA025953, AW135690, BF820542, BF737942, AA371827, N90491, H66699, BG012708, H64951, D31533, BE769806, AA368991, H01130, N69227, H01871, H89819, BF821339, R72785, BE769826, R62666, N45434, BF349116, R72786, AW374237, AW953834, T16823, AA295668, BE140683, AW277068, AI872250, AI088641, H78057, H73228, BF881707, AW374232, AW610099, R24669, H26462, AI202813, T23681, T72232, H27838, H64952, BE769808, H70128, N47826, R43349, AI281745, H83150, AI476021, BF991147, BF338495, AW605902, AW105588, BF920649, AW085673, AW082623, BE011964, R17629, AI281707, AL514409, AI628316, AL513817, AI925156, AW087534, H27773, AW083175, AW188539, AI420521, AI621209, AI859429, AI554821, BF812938, AI697188, AI632033, BE905366, AI874109, AW075413, AI251434, AA833760, AI635478, AI684036, BG121959, AI571861, AI824648, BE965053, AI569945, AI566003, AI669609, AI680435, AI828818, AA449768, AI572787, AI653541, AW087160, AI475134, BE895765, AL514867, AW079654, AI923357, AI587056, AI654672, AL514579, AI912434, AL513723, BE964078, AI249962, AL513809, AI817552, AX040958, AL359615, AF155148, AK026630, AB034701, AL162083, AF218034, AB044560, Z82022, AF026008, AL133606, AK000083, AK026651, AX040974, AL117435,

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77	HLYFJ90	87	1243873	AW629186, W58365, W80353, AA707514, AI571382, AA677325, AA527041, AI697493, AA150417, AA844727, AI190775, AI192166, AI831081, AA148817, AA704578, AA136471, N98481, AA552027, W24254, AI198260, H22060, AI307308, W86084, AA781837, N92868, AA136961, AI052084, AI917791, AI149607, AI308164, AI933238, AA551635, AI568102, F22559, BF059641, AI027845, AI263395, R09685, AI370711, AA902877, R09684, AW362086, AA648096, AA913295, AI468042, W25594, AA493101, AL121078, BF913273, AA865211, AA913724, W78949, BE503336, AW881520, BG249582, BG164558, BG166654, BF527014, AV708075, BE047852, BG177717, AW149925, BF525578, AA580663, BE891834, AL041150, BG121959, AI623179, BE880190, AW169604, AL037454, BG058150, AI802240, AI307494, BF343174, BG034646, BF965877, AL036980, BG179355, AI345347, BF037975, AI345416, BE910373, AI345612, BF037097, AI310575, AI567582, AI345415, AA916133, AI890507, AI366968, AL079963, BG107576, BE874133, AI889953, AI340533, AW073994, BF033757, AI366959, AI686964, BF814761, AV656903, AL036631, BF968017, AI468872, AL036673, AW827206, AI500061, AI670009, AI698391, AI345005, BE138658, AV653297, BG255465, BE622183, AA225339, BE778198, BF970658, AW151136, AI287326, AI335338, AL047344, AW020561, BG251104, AI917994, BF892007, AI335426, AA421957, AI348777, AW071362, BF344705, AW301300, AW827193, AW075207, BF814420, AL048323, AW806761, AI365256, AI343037, AI366549, AW827228, AI335363, AL048340, BG028563, AL048656, BG029053, AI923989, AI254731, AW167918, AI349186, AI307543, BE965169, AI345557, AL119791, BG178911, AW071395, AI340659, AI345253, AI753683, AW269097, AW161579, AI312428, AI340644, AI311892, BE739277, AI307736, BF814357, AW020693, BG031664, BG030364, AI349266, AI310592, AI348897, BE778453, BG058217, AI862144, AI689420, AV724898, AI866770, BE876394, BG001235, AI690748, BE885353, BE969227, AI310920, AW827289, AW163834, AL118781, BG112718, AI345608, AW020095, AW302965, AV713580, BF525853, BF792180, AW059828, AV681759, AL036265, BE789764, BF816042, AV757035, BG179993, AW301513, AL037582, AV657079, AL037602, BF343391, AI307503, BF970362, BF344691, BG179078, BG029667, BF812960, AI340537, AI336634, AI307459, AI554245, AW071276, AW162189, AL121463, AL047422, AL042544, AL119748, AI473536, AI571439, AV652906, AL048871, AV721521, BE964078, AV649810,

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				AF230496, AL389935, AF111112, AB019565, AL122049, AL137526, AF097996, AF119875, Y11254, AK000445, AL049466, AF130100, AL117583, AK025084, AB048954, AK027213, AL117585, AK027200, A93350, AL110221, AL162062, AF130075, AF125948, AB049758, AL096744, AL133077, AX010492, AL050108, AL359618, AL050393, AL133072, U42766, S78214, AK026608, AL122123, AK026462, AF130059, E07361, and U00763.
77	HLYFJ90	190	1218626	AW629186, W58365, W80353, AA707514, AA677325, AI571382, AI697493, AA150417, AA527041, AA844727, AI190775, AI192166, AA148817, AI831081, N98481, AA136471, AA704578, AA552027, W24254, AI198260, H22060, W86084, AA781837, AA136961, N92868, AI052084, AI917791, AI149607, AI307308, AI933238, AA551635, AI308164, AI568102, F22559, AI027845, BF059641, R09685, AI370711, AI263395, R09684, AA902877, AW362086, AA648096, AA913295, AI468042, W25594, AA493101, BF913273, AL121078, AA865211, W78949, AA913724, BE503336, AW881520, R78164, and AI906039.
78	HMLHD54	88	1243834	AL525815, AL513933, BE613037, AL513934, AL525855, BE907046, AA680328, AL531478, AL531477, AI086068, BE881149, BF034542, AI808996, BE876417, AI472146, BG179117, BE873774, AW189572, AW439178, AI623450, AL528905, AI612758, BE710393, AI472067, AW117897, AI554566, AW189151, AA085582, BE785258, AA554828, BF431916, BF430973, W52490, AA526837, BE734344, BF590357, BE260921, BE927705, AW339734, BE620493, AA161483, BE962575, AW304916, BG254861, BG028029, AI536777, AA913459, BE612357, AA533037, AA234924, BE881738, BE898403, BE733539, AW468992, BE897519, AW886502, BE622014, AA643610, AA151194, BE834385, BE967212, AA706596, AW959302, BF744358, AI634597, BE710446, BF745246, AA234925, AI208156, BF744357, BE278764, BF744648, AW838915, AI459828, BE272744, AI358324, BE710474, AW938825, AW189865, AI929467, AI452700, AA233379, N41687, AV688903, AI358564, AI684134, AI868628, BF939149, BF895375, BE737207, AA724153, AI928985, AA666281, AI300741, AA865704, AI435019, AW881424, AI433265, AA102021, BG107509, AA085714, AW603389, AI816245, AI816324, BG252911, AI249273, AA948064, AA233012, T95929, BF802517, N28668, AA504539, BE880085, BF809912, AA301441, BF803201, BF745257, AW886516, BF747102, BF803200, T95834, AA913442, BF850106, AA533751, BF919530, C21380, AI565199, BF850102, BF959271, BF958073, AA844821, AA905209,

				BF958074, BF850090, BF850098, BF959267, BF109084, AI919584, BE934981, AI539681, BE837584, BF837464, AA348086, AW886722, AI620671, AA160955, AI381669, BF837462, BF747103, AA583023, and AL031320.
78	HMLHD54	191	1214441	AL525855, AL513934, AL531478, AL528905, BE734344, BE620493, BG254861, BE612357, BE881738, BE733539, BE622014, BE897519, BE898403, BE737207, BE278764, BE260921, BE272744, AI929467, AW938825, BF745246, BF744358, BE907046, BG028029, BG179117, BF744357, AI928985, BF744648, AA102021, AA085714, AI816324, AW603389, BG252911, N28668, AA504539, BF745257, BF747102, AA348086, AL525815, AA160955, BE881149, AW838915, BE873774, BE710393, BF034542, and AL031320.
79	HBPOM70	89	1283382	AW368451, BF943652, AA099385, AA099386, AA029791, AA029790, BE145192, W38789, AA378020, AA411303, and R81402.
79	HBPOM70	192	1210399	AW368451, BE222668, BF057062, BF059422, BF943652, AA417890, AA099385, AW236145, AW471449, AI276742, AI766890, AA099386, N78573, W07168, AA001874, W79183, AA436249, AW292407, AA055463, AA482460, AI252807, AI266170, W74429, BF476100, AI167320, N93113, AA029791, AA055462, AI536067, AW003037, AA411303, AA404452, H25100, AW296497, AW236004, AA001796, AA029790, BE145192, W38789, AA831374, BE833432, H24895, R81403, R81402, AA993005, AA378020, AW235742, AI078078, and N58979.
80	HMSMO35	90	1243922	AV714931, AA708108, BE541237, AL138293, AU140403, AV760760, AV700663, BE796439, AV699393, BE538259, BF872337, AA577824, BG260565, AV722030, AV762220, AV734401, BF826830, BF915799, AV760723, AU154050, AV762129, BE300645, BF828714, AV722075, BF892846, BE566072, AL048626, AU147226, AL135377, AA486896, AA708751, AU144517, AA524604, BE867712, AL524262, AV699423, AA481760, AV762783, BF574637, AU123691, AV700654, AL079869, AW963473, AW963982, AW504485, AW407632, BE394939, AU117926, AA608588, AA640277, AW085751, BF528078, BF902291, BF736198, AA608612, AI866487, BE075868, AW405593, AA613257, AI114591, AA315361, AL080314, AC005231, AC009362, AC005081, AF111169, AC002477, AC005736, AL031311, AC004089, AC005520, AL109825, AL050349, AC005015, Z93023, AP001630, AP001711, AC004166, AC006509, AC016395, AC007868, AC008155, AL031848, AC003036, Z99716, AC009086, AC011465, AC020934, AL121900, AJ277546, AC020913, AC005619, AL109613, AC005037, AL022320, AP001748, AL049830, AC004491, AL024507, AC007345,

				AC008738, AC011469, U62293, AL138721, AC011479, AL049832, AC002425, AL049829, AL121653, AP000500, AL049569, AP001725, AC018720, AP001752, AC005098, AC004922, AL121771, AC004966, AC006337, AL031390, AC006329, AL035587, AC008066, AC004884, AC008760, AC016027, AL049776, AP001717, AC005839, AL035404, AP001727, AC018663, AC022392, AF196970, AC007182, AC005529, AC005102, AC007226, AC027319, AP000694, AC004893, AL022237, AC020552, AC006449, AL050335, AL136172, Z82172, AC016830, AL121897, AL121658, AC011491, AC068799, AC009298, AC007999, AL024498, AL353574, Z97054, AL049537, AC004542, AC007383, AC005527, AF001549, AL033529, AC004876, D87675, AC021016, Z94801, AC020916, AL121585, AP001710, AC004834, AC020550, AC007842, AC005669, AC008569, AL031281, AC008403, AF235097, AL079335, AP000555, AC002400, Z93930, AC004217, AC007263, Z84469, AL034417, AL031735, AC005726, AC002350, AL137129, AP001208, AC023425, AC000025, AC007938, AC006345, AC008521, AL117380, AC002418, AC006111, AC010458, AC011489, AL109797, AL050318, AP001330, AC020904, AC006483, AC009470, AC004965, AF111168, AL109963, AL354872, AC009955, AC007308, AL132777, AC005632, AC006011, AL499628, AF124523, AL133448, AC007327, AL049795, AL022163, AL031737, AP000030, AC004084, AC005089, AC011480, AL353804, AL133215, U91323, AL035086, AC004656, AC007225, AC008745, AC005522, AC007956, AL137818, AF196969, AC004819, AE000658, AL161445, AC009311, AL022328, AL139353, AC007954, AL080243, AL035461, U91321, AC008736, AC005837, AL035683, AL139339, AL161781, AC008616, AC004125, AC006014, AC004867, AC006312, AL117336, AL022476, AC007151, AC005295, AC005887, AL022323, AC012384, AC025588, AC008750, AC007957, AC004659, AC003101, AC007850, AC005531, AC018644, AL034420, AB023050, AC025593, AL009181, AC007172, Z95115, AL136137, AC005944, AL078581, AC006121, AC008784, AC011495, AP001753, AC009244, AC004990, AP000212, AP000134, AL133288, AL031005, AC010618, AL021391, AC011452, AL132765, AP000553, Z84466, AC006965, AL023553, AC009002, AC005952, AC007363, AC011490, AP000353, AC011464, AL034429, AC005695, AL135839, AC005488, and AP001759.
81	HMUCI88	91	1256397	AI670100, AL040592, AW192857, AI924560, AI745172, AI554795, R43941, AI815747, AI016875, BF445691, BF445690, T15732, T17119, AI301252, BF038572, AA665984, AI819865,

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81	HMUCI88	194	1209766	BE408692, BE867639, BE294258, BE294711, AI670100, AW954563, BF732613, BF111894, BE675998, AI453554, AL040592, AI183347, AA769112, AW007124, AI275597, AL040591, AI924560, AI830912, AW026311, W03018, AI141179, BG169470, BF059042, AA847666, AI690200, BF440020, N21662, BG150026, AI340038, AI745172, AW192857, AI052646, AI017823, AI554795, BF446007, BF688795, AI860464, AI570410, AA393934, AI374791, AI366708, BF449025, AI815747, W72235, AI016875, AI343003, AW965580, W76472, N72276, AW001484, N68988, BF445994, BF445691, AI022212, R48114, W60501, BF445690, AI684578, W69293, AA456766, R84578, AW297598, N27124, T17119, BE818146, AI830849, T15732, BF477844, H24887, AI819865, BF829877, AA665984, AI301252, AA216704, AA954544, H11531, R43941, AI815941, H93511, AA746046, H51177, W69294, BF058775, AW166780, N40060, T33270, W15272, Z44718, BF038572, R13995, BE836928, H84314, AA829386, T08615, AW072981, H41501, H39684, AA988034, N76401, H11424, BF477587, AW968809, BE220204, W25654, R18830, AI352230, R40213, R69605, H21592, H97176, BF447396, BG000118, AA489679, BE871213, H42932, AW247730, BF745393, R47999, W02701, BE836925, BF811125, AI628723, W39233, AA748168, BE041494, AI336273, AW451867, T33269, BE246910, BF001903, AW732072, H25086, AI758366, AW614134, AA824466, BE000406, AW452112, BE206969, AA877559, AA458940, H21513, R39118, BE466544, BF514031, BE836910, AI016657, BE836903, AW469146, and M94721.
82	HMUDN51	92	1275158	BE732224, AW025604, AW963839, AI344048, BE042489, AW025605, AI732328, H78941, AI768505, AW884213, AA371876, AA862436, AA587744, T97673, AW750816, AU159322, AI033275, BE175100, BG248789, AW087466, AA375852, BE041287, BE159584, AA860560, BF809952, AK023937, and AB014607.
82	HMUDN51	195	1209998	BE732224, AK023937, and AB014607.
83	HMAGC36	93	1262016	AI990481, AI090193, AW245081, AI143992, AI598190, AI859137, AI350501, AA495832, AI361951, AI990174, AI380542, AW003834, AA994262, AW025153, AI394639, AI086091, AA976745, AA293019, AA417706, BE727402,

				AI351614, AI202144, AA495776, W00431, AA253139, AA115762, R88936, N72164, AW237082, R90773, AI766469, AI672360, BF718243, AA745682, AW134904, F23330, AL119175, AW268196, AI913519, AW274357, R36266, AA133537, AA113803, AA496881, AA610858, AA417588, AI685216, AW072885, AW966703, AA326898, AA114066, AA344498, AA248795, AW474388, BE252368, AA905473, BF222472, BG060006, BF755528, BG112348, BF895218, AF218008, AC005787, and AC005786.
83	HMAGC36	196	1219629	AI990481, AI138384, AI090193, AI859137, AI598190, AW245081, AI350501, AI143992, AW003834, AI032285, AW025153, AI990174, AA495832, AI361951, AA994262, AI086091, AI041269, AA417706, AI380542, AI394639, AA495776, AA976745, AA293019, BG029787, BE872513, AA253139, AI183841, W00431, AI351614, BE727402, AW237082, R88936, AA115762, AI202144, N72164, R90773, AI766469, AL119175, BF718243, AA745682, AA725758, AI672360, AA113803, AW134904, F23330, BF829762, AA133537, AI913519, R36266, BE410356, AA496881, AW274357, AW268196, AA610858, AW072885, AI685216, AW966703, AA417588, AA326898, AA344498, AA248795, AA114066, BF744645, AW474388, BE277069, BE252368, BE408266, AA906034, BF755528, AC005786, AC005787, AF218008, and R36265.
83	HMAGC36	197	1219632	BF689868, BF027339, BE791172, BE273437, BE260092, BG031379, BF339469, BF984194, AI760572, AI760520, BE676312, BE294301, AW297966, AW245081, AA495832, AI090193, AI361951, AA962223, AI244284, AI143992, AI598190, AI990174, AI380542, AI422554, AI859137, AI350501, AA994262, AI990481, AI971830, AI394639, AI086091, BF975689, BE383741, AW003834, AA976745, BE252368, AA293019, AA644162, AI351614, AA253139, N50101, AW136878, AA115762, AI813447, AI732960, BF059508, AW070837, AW246650, R88936, AI202144, AW237082, N72164, AA862886, AW190926, AW025153, R90773, BE727402, BF027207, AI766469, AW129676, AI672360, BF718243, AA745682, AW134904, AL119175, BF690095, N33565, AA495776, F23330, AA417706, BF869114, AI913519, AI284384, AW268196, AW274357, R36266, W00431, BE408877, AA496881, BE159093, BE410963, AA610858, AA417588, AI582214, BG060127, AI685216, BG033163, AW072885, W70088, BE546341, BF222472, AA905473, BG060006, BF691868, AA082841, AA114066, AW474388, BF745906, AA133537, AI000915, AA293473, AI693690, AW971745, AA326898, AA248795, AW861944, AW804686, BF755528,

				AW392670, AW966703, BE695785, AL119401, BF763934, AW604723, AA344498, BE705903, AW858526, BE705906, AW372827, AW858525, AW577135, AL134902, AW384394, U46351, AW861889, AW858455, AL119443, AW363220, AL119497, AL119319, AL119457, AL119341, AL119355, AL119324, BF868697, AL119396, U46341, AL119522, Z99396, AW877209, AL119483, AL042433, AL119484, AL119363, AL119391, U46350, U46347, U46349, BE705905, AL119335, AL119444, U46346, BF868684, AL134536, AL037205, AL042614, AW604726, BF868687, AL119439, AI142132, BE705904, AL119399, AL119496, AL134525, AW861954, AL134524, U46345, AL119418, AL043019, AL134527, AL042450, AL134538, AL042544, AL042978, AL042896, AI142137, AL042965, AL042975, AL042970, AL042542, AL042984, AI142139, AL043029, AL042551, AL043003, AB033068, AC005786, AC005787, AF218008, AR080280, AB026436, AR054110, AJ251859, AX030435, AR066494, A81671, AR060234, AR069079, AX046357, and AJ279014.

Table 4

Code	Description	Tissue	Organ	Cell Line	Disease	Vector
AR022	a_Heart	a_Heart				
AR023	a_Liver	a_Liver				
AR024	a_mammary gland	a_mammary gland				
AR025	a_Prostate	a_Prostate				
AR026	a_small intestine	a_small intestine				
AR027	a_Stomach	a_Stomach				
AR028	Blood B cells	Blood B cells				
AR029	Blood B cells activated	Blood B cells activated				
AR030	Blood B cells resting	Blood B cells resting				
AR031	Blood T cells activated	Blood T cells activated				
AR032	Blood T cells resting	Blood T cells resting				
AR033	brain	brain				
AR034	breast	breast				
AR035	breast cancer	breast cancer				
AR036	Cell Line CAOV3	Cell Line CAOV3				
AR037	cell line PA-1	cell line PA-1				
AR038	cell line transformed	cell line transformed				
AR039	colon	colon				
AR040	colon (9808co65R)	colon (9808co65R)				
AR041	colon (9809co15)	colon (9809co15)				
AR042	colon cancer	colon cancer				
AR043	colon cancer (9808co64R)	colon cancer (9808co64R)				
AR044	colon cancer 9809co14	colon cancer				

		9809co14				
AR045	corn clone 5	corn clone 5				
AR046	corn clone 6	corn clone 6				
AR047	corn clone2	corn clone2				
AR048	corn clone3	corn clone3				
AR049	Corn Clone4	Corn Clone4				
AR050	Donor II B Cells 24hrs	Donor II B Cells 24hrs				
AR051	Donor II B Cells 72hrs	Donor II B Cells 72hrs				
AR052	Donor II B-Cells 24 hrs.	Donor II B-Cells 24 hrs.				
AR053	Donor II B-Cells 72hrs	Donor II B-Cells 72hrs				
AR054	Donor II Resting B Cells	Donor II Resting B Cells				
AR055	Heart	Heart				
AR056	Human Lung (clonetech)	Human Lung (clonetech)				
AR057	Human Mammary (clontech)	Human Mammary (clontech)				
AR058	Human Thymus (clonetech)	Human Thymus (clonetech)				
AR059	Jurkat (unstimulated)	Jurkat (unstimulated)				
AR060	Kidney	Kidney				
AR061	Liver	Liver				
AR062	Liver (Clontech)	Liver (Clontech)				
AR063	Lymphocytes chronic lymphocytic leukaemia	Lymphocytes chronic lymphocytic leukaemia				

AR064	Lymphocytes diffuse large B cell lymphoma	Lymphocytes diffuse large B cell lymphoma				
AR065	Lymphocytes follicular lymphoma	Lymphocytes follicular lymphoma				
AR066	normal breast	normal breast				
AR067	Normal Ovarian (4004901)	Normal Ovarian (4004901)				
AR068	Normal Ovary 9508G045	Normal Ovary 9508G045				
AR069	Normal Ovary 9701G208	Normal Ovary 9701G208				
AR070	Normal Ovary 9806G005	Normal Ovary 9806G005				
AR071	Ovarian Cancer	Ovarian Cancer				
AR072	Ovarian Cancer (9702G001)	Ovarian Cancer (9702G001)				
AR073	Ovarian Cancer (9707G029)	Ovarian Cancer (9707G029)				
AR074	Ovarian Cancer (9804G011)	Ovarian Cancer (9804G011)				
AR075	Ovarian Cancer (9806G019)	Ovarian Cancer (9806G019)				
AR076	Ovarian Cancer (9807G017)	Ovarian Cancer (9807G017)				
AR077	Ovarian Cancer (9809G001)	Ovarian Cancer (9809G001)				
AR078	ovarian cancer 15799	ovarian cancer 15799				
AR079	Ovarian Cancer 17717AID	Ovarian Cancer 17717AID				

AR080	Ovarian Cancer 4004664B1	Ovarian Cancer 4004664B1				
AR081	Ovarian Cancer 4005315A1	Ovarian Cancer 4005315A1				
AR082	ovarian cancer 94127303	ovarian cancer 94127303				
AR083	Ovarian Cancer 96069304	Ovarian Cancer 96069304				
AR084	Ovarian Cancer 9707G029	Ovarian Cancer 9707G029				
AR085	Ovarian Cancer 9807G045	Ovarian Cancer 9807G045				
AR086	ovarian cancer 9809G001	ovarian cancer 9809G001				
AR087	Ovarian Cancer 9905C032RC	Ovarian Cancer 9905C032RC				
AR088	Ovarian cancer 9907 C00 3rd	Ovarian cancer 9907 C00 3rd				
AR089	Prostate	Prostate				
AR090	Prostate (clonetech)	Prostate (clonetech)				
AR091	prostate cancer	prostate cancer				
AR092	prostate cancer #15176	prostate cancer #15176				
AR093	prostate cancer #15509	prostate cancer #15509				
AR094	prostate cancer #15673	prostate cancer #15673				
AR095	Small Intestine (Clontech)	Small Intestine (Clontech)				
AR096	Spleen	Spleen				
AR097	Thymus T cells activated	Thymus T cells				

		activated				
AR098	Thymus T cells resting	Thymus T cells resting				
AR099	Tonsil	Tonsil				
AR100	Tonsil geminal center centroblast	Tonsil geminal center centroblast				
AR101	Tonsil germinal center B cell	Tonsil germinal center B cell				
AR102	Tonsil lymph node	Tonsil lymph node				
AR103	Tonsil memory B cell	Tonsil memory B cell				
AR104	Whole Brain	Whole Brain				
AR105	Xenograft ES-2	Xenograft ES-2				
AR106	Xenograft SW626	Xenograft SW626				
H0002	Human Adult Heart	Human Adult Heart	Heart			Uni-ZAP XR
H0008	Whole 6 Week Old Embryo					Uni-ZAP XR
H0009	Human Fetal Brain					Uni-ZAP XR
H0011	Human Fetal Kidney	Human Fetal Kidney	Kidney			Uni-ZAP XR
H0012	Human Fetal Kidney	Human Fetal Kidney	Kidney			Uni-ZAP XR
H0013	Human 8 Week Whole Embryo	Human 8 Week Old Embryo	Embryo			Uni-ZAP XR
H0014	Human Gall Bladder	Human Gall Bladder	Gall Bladder			Uni-ZAP XR
H0015	Human Gall Bladder, fraction II	Human Gall Bladder	Gall Bladder			Uni-ZAP XR
H0022	Jurkat Cells	Jurkat T-Cell Line				Lambda ZAP II
H0024	Human Fetal Lung III	Human Fetal Lung	Lung			Uni-ZAP XR
H0026	Namalwa Cells	Namalwa B-Cell Line, EBV				Lambda ZAP II

		immortalized				
H0031	Human Placenta	Human Placenta	Placenta			Uni-ZAP XR
H0032	Human Prostate	Human Prostate	Prostate			Uni-ZAP XR
H0036	Human Adult Small Intestine	Human Adult Small Intestine	Small Int.			Uni-ZAP XR
H0038	Human Testes	Human Testes	Testis			Uni-ZAP XR
H0039	Human Pancreas Tumor	Human Pancreas Tumor	Pancrea s		disease	Uni-ZAP XR
H0040	Human Testes Tumor	Human Testes Tumor	Testis		disease	Uni-ZAP XR
H0041	Human Fetal Bone	Human Fetal Bone	Bone			Uni-ZAP XR
H0042	Human Adult Pulmonary	Human Adult Pulmonary	Lung			Uni-ZAP XR
H0046	Human Endometrial Tumor	Human Endometrial Tumor	Uterus		disease	Uni-ZAP XR
H0050	Human Fetal Heart	Human Fetal Heart	Heart			Uni-ZAP XR
H0051	Human Hippocampus	Human Hippocampus	Brain			Uni-ZAP XR
H0052	Human Cerebellum	Human Cerebellum	Brain			Uni-ZAP XR
H0056	Human Umbilical Vein, Endo. remake	Human Umbilical Vein Endothelial Cells	Umbilic al vein			Uni-ZAP XR
H0057	Human Fetal Spleen					Uni-ZAP XR
H0059	Human Uterine Cancer	Human Uterine Cancer	Uterus		disease	Lambda ZAP II
H0063	Human Thymus	Human Thymus	Thymus			Uni-ZAP XR
H0068	Human Skin Tumor	Human Skin Tumor	Skin		disease	Uni-ZAP XR
H0069	Human Activated T-Cells	Activated T-Cells	Blood	Cell Line		Uni-ZAP XR
H0078	Human Lung Cancer	Human Lung Cancer	Lung		disease	Lambda ZAP II
H0083	HUMAN JURKAT	Jurkat Cells				Uni-ZAP XR

	MEMBRANE BOUND POLYSOMES					
H0086	Human epithelioid sarcoma	Epithelioid Sarcoma, muscle	Sk Muscle		disease	Uni-ZAP XR
H0087	Human Thymus	Human Thymus				pBluescript
H0090	Human T-Cell Lymphoma	T-Cell Lymphoma	T-Cell		disease	Uni-ZAP XR
H0100	Human Whole Six Week Old Embryo	Human Whole Six Week Old Embryo	Embryo			Uni-ZAP XR
H0102	Human Whole 6 Week Old Embryo (II), subt	Human Whole Six Week Old Embryo	Embryo			pBluescript
H0111	Human Placenta, subtracted	Human Placenta	Placenta			pBluescript
H0122	Human Adult Skeletal Muscle	Human Skeletal Muscle	Sk Muscle			Uni-ZAP XR
H0123	Human Fetal Dura Mater	Human Fetal Dura Mater	Brain			Uni-ZAP XR
H0124	Human Rhabdomyosarcoma	Human Rhabdomyosarcoma	Sk Muscle		disease	Uni-ZAP XR
H0125	Cem cells cyclohexamide treated	Cyclohexamide Treated Cem, Jurkat, Raji, and Supt	Blood	Cell Line		Uni-ZAP XR
H0129	Jurkat cells, thiouridine activated, fract II	Jurkat Cells				Uni-ZAP XR
H0131	LNCAP + o.3nM R1881	LNCAP Cell Line	Prostate	Cell Line		Uni-ZAP XR
H0134	Raji Cells, cyclohexamide treated	Cyclohexamide Treated Cem, Jurkat, Raji, and Supt	Blood	Cell Line		Uni-ZAP XR
H0135	Human Synovial Sarcoma	Human Synovial Sarcoma	Synovium			Uni-ZAP XR
H0136	Supt Cells, cyclohexamide treated	Cyclohexamide Treated Cem, Jurkat,	Blood	Cell Line		Uni-ZAP XR

		Raji, and Supt				
H0144	Nine Week Old Early Stage Human	9 Wk Old Early Stage Human	Embryo			Uni-ZAP XR
H0149	7 Week Old Early Stage Human, subtracted	Human Whole 7 Week Old Embryo	Embryo			Uni-ZAP XR
H0156	Human Adrenal Gland Tumor	Human Adrenal Gland Tumor	Adrenal Gland		disease	Uni-ZAP XR
H0159	Activated T-Cells, 8 hrs., ligation 2	Activated T-Cells	Blood	Cell Line		Uni-ZAP XR
H0163	Human Synovium	Human Synovium	Synoviu m			Uni-ZAP XR
H0164	Human Trachea Tumor	Human Trachea Tumor	Trachea		disease	Uni-ZAP XR
H0169	Human Prostate Cancer, Stage C fraction	Human Prostate Cancer, stage C	Prostate		disease	Uni-ZAP XR
H0170	12 Week Old Early Stage Human	Twelve Week Old Early Stage Human	Embryo			Uni-ZAP XR
H0171	12 Week Old Early Stage Human, II	Twelve Week Old Early Stage Human	Embryo			Uni-ZAP XR
H0176	CAMA1Ee Cell Line	CAMA1Ee Cell Line	Breast	Cell Line		Uni-ZAP XR
H0177	CAMA1Ee Cell Line	CAMA1Ee Cell Line	Breast	Cell Line		Uni-ZAP XR
H0178	Human Fetal Brain	Human Fetal Brain	Brain			Uni-ZAP XR
H0179	Human Neutrophil	Human Neutrophil	Blood	Cell Line		Uni-ZAP XR
H0180	Human Primary Breast Cancer	Human Primary Breast Cancer	Breast		disease	Uni-ZAP XR
H0181	Human Primary Breast Cancer	Human Primary Breast Cancer	Breast		disease	Uni-ZAP XR
H0184	Human Colon Cancer, metasticized to live	Human Colon Cancer, metasticized	Liver		disease	Lambda ZAP II

		to liver				
H0194	Human Cerebellum, subtracted	Human Cerebellum	Brain			pBluescript
H0196	Human Cardiomyopathy, subtracted	Human Cardiomyopathy	Heart			Uni-ZAP XR
H0197	Human Fetal Liver, subtracted	Human Fetal Liver	Liver			Uni-ZAP XR
H0204	Human Colon Cancer, subtracted	Human Colon Cancer	Colon			pBluescript
H0208	Early Stage Human Lung, subtracted	Human Fetal Lung	Lung			pBluescript
H0213	Human Pituitary, subtracted	Human Pituitary				Uni-ZAP XR
H0222	Activated T-Cells, 8 hrs, subtracted	Activated T-Cells	Blood	Cell Line		Uni-ZAP XR
H0231	Human Colon, subtraction	Human Colon				pBluescript
H0232	Human Colon, differential expression	Human Colon				pBluescript
H0235	Human colon cancer, metaticized to liver, subtraction	Human Colon Cancer, metasticized to liver	Liver			pBluescript
H0244	Human 8 Week Whole Embryo, subtracted	Human 8 Week Old Embryo	Embryo			Uni-ZAP XR
H0250	Human Activated Monocytes	Human Monocytes				Uni-ZAP XR
H0251	Human Chondrosarcoma	Human Chondrosarcoma	Cartilage		disease	Uni-ZAP XR
H0252	Human Osteosarcoma	Human Osteosarcoma	Bone		disease	Uni-ZAP XR
H0253	Human adult testis, large inserts	Human Adult Testis	Testis			Uni-ZAP XR

H0254	Breast Lymph node cDNA library	Breast Lymph Node	Lymph Node			Uni-ZAP XR
H0255	breast lymph node CDNA library	Breast Lymph Node	Lymph Node			Lambda ZAP II
H0256	HL-60, unstimulated	Human HL-60 Cells, unstimulated	Blood	Cell Line		Uni-ZAP XR
H0261	H. cerebellum, Enzyme subtracted	Human Cerebellum	Brain			Uni-ZAP XR
H0263	human colon cancer	Human Colon Cancer	Colon		disease	Lambda ZAP II
H0264	human tonsils	Human Tonsil	Tonsil			Uni-ZAP XR
H0265	Activated T-Cell (12hs)/Thiouridine labelledEco	T-Cells	Blood	Cell Line		Uni-ZAP XR
H0266	Human Microvascular Endothelial Cells, fract. A	HMEC	Vein	Cell Line		Lambda ZAP II
H0268	Human Umbilical Vein Endothelial Cells, fract. A	HUVE Cells	Umbilical vein	Cell Line		Lambda ZAP II
H0270	HPAS (human pancreas, subtracted)	Human Pancreas	Pancreas			Uni-ZAP XR
H0271	Human Neutrophil, Activated	Human Neutrophil - Activated	Blood	Cell Line		Uni-ZAP XR
H0272	HUMAN TONSILS, FRACTION 2	Human Tonsil	Tonsil			Uni-ZAP XR
H0284	Human OB MG63 control fraction I	Human Osteoblastoma MG63 cell line	Bone	Cell Line		Uni-ZAP XR
H0286	Human OB MG63 treated (10 nM E2) fraction I	Human Osteoblastoma MG63 cell line	Bone	Cell Line		Uni-ZAP XR
H0288	Human OB HOS control	Human	Bone	Cell Line		Uni-ZAP XR

	fraction I	Osteoblastoma HOS cell line				
H0290	Human OB HOS treated (1 nM E2) fraction I	Human Osteoblastoma HOS cell line	Bone	Cell Line		Uni-ZAP XR
H0292	Human OB HOS treated (10 nM E2) fraction I	Human Osteoblastoma HOS cell line	Bone	Cell Line		Uni-ZAP XR
H0293	WI 38 cells					Uni-ZAP XR
H0294	Amniotic Cells - TNF induced	Amniotic Cells - TNF induced	Placenta	Cell Line		Uni-ZAP XR
H0295	Amniotic Cells - Primary Culture	Amniotic Cells - Primary Culture	Placenta	Cell Line		Uni-ZAP XR
H0305	CD34 positive cells (Cord Blood)	CD34 Positive Cells	Cord Blood			ZAP Express
H0306	CD34 depleted Buffy Coat (Cord Blood)	CD34 Depleted Buffy Coat (Cord Blood)	Cord Blood			ZAP Express
H0309	Human Chronic Synovitis	Synovium, Chronic Synovitis/ Osteoarthritis	Synoviu m		disease	Uni-ZAP XR
H0318	HUMAN B CELL LYMPHOMA	Human B Cell Lymphoma	Lymph Node		disease	Uni-ZAP XR
H0320	Human frontal cortex	Human Frontal Cortex	Brain			Uni-ZAP XR
H0327	human corpus colosum	Human Corpus Callosum	Brain			Uni-ZAP XR
H0328	human ovarian cancer	Ovarian Cancer	Ovary		disease	Uni-ZAP XR
H0331	Hepatocellular Tumor	Hepatocellular Tumor	Liver		disease	Lambda ZAP II
H0333	Hemangiopericytoma	Hemangiopericytom	Blood		disease	Lambda ZAP

		a	vessel			II
H0340	Corpus Callosum	Corpus Collosum-93052				Uni-ZAP XR
H0341	Bone Marrow Cell Line (RS4;11)	Bone Marrow Cell Line RS4;11	Bone Marrow	Cell Line		Uni-ZAP XR
H0351	Glioblastoma	Glioblastoma	Brain		disease	Uni-ZAP XR
H0352	wilm"s tumor	Wilm"s Tumor			disease	Uni-ZAP XR
H0354	Human Leukocytes	Human Leukocytes	Blood	Cell Line		pCMVSport 1
H0355	Human Liver	Human Liver, normal Adult				pCMVSport 1
H0363	Human Brain Medulla, subtracted	Human Brain Medulla				pBluescript
H0369	H. Atrophic Endometrium	Atrophic Endometrium and myometrium				Uni-ZAP XR
H0370	H. Lymph node breast Cancer	Lymph node with Met. Breast Cancer			disease	Uni-ZAP XR
H0373	Human Heart	Human Adult Heart	Heart			pCMVSport 1
H0375	Human Lung	Human Lung				pCMVSport 1
H0376	Human Spleen	Human Adult Spleen	Spleen			pCMVSport 1
H0381	Bone Cancer	Bone Cancer			disease	Uni-ZAP XR
H0383	Human Prostate BPH, re-excision	Human Prostate BPH				Uni-ZAP XR
H0386	Leukocyte and Lung; 4 screens	Human Leukocytes	Blood	Cell Line		pCMVSport 1
H0392	H. Meningima, M1	Human Meningima	brain			pSport1
H0393	Fetal Liver, subtraction II	Human Fetal Liver	Liver			pBluescript
H0400	Human Striatum Depression, re-rescue	Human Brain, Striatum Depression	Brain			Lambda ZAP II
H0402	CD34 depleted Buffy Coat	CD34 Depleted	Cord			ZAP Express

	(Cord Blood), re-excision	Buffy Coat (Cord Blood)	Blood			
H0409	H. Striatum Depression, subtracted	Human Brain, Striatum Depression	Brain			pBluescript
H0411	H Female Bladder, Adult	Human Female Adult Bladder	Bladder			pSport1
H0412	Human umbilical vein endothelial cells, IL-4 induced	HUVE Cells	Umbilical vein	Cell Line		pSport1
H0413	Human Umbilical Vein Endothelial Cells, uninduced	HUVE Cells	Umbilical vein	Cell Line		pSport1
H0414	Ovarian Tumor I, OV5232	Ovarian Tumor, OV5232	Ovary		disease	pSport1
H0416	Human Neutrophils, Activated, re-excision	Human Neutrophil - Activated	Blood	Cell Line		pBluescript
H0421	Human Bone Marrow, re-excision	Bone Marrow				pBluescript
H0422	T-Cell PHA 16 hrs	T-Cells	Blood	Cell Line		pSport1
H0423	T-Cell PHA 24 hrs	T-Cells	Blood	Cell Line		pSport1
H0424	Human Pituitary, subt IX	Human Pituitary				pBluescript
H0427	Human Adipose	Human Adipose, left hiplipoma				pSport1
H0428	Human Ovary	Human Ovary Tumor	Ovary			pSport1
H0429	K562 + PMA (36 hrs),re-excision	K562 Cell line	cell line	Cell Line		ZAP Express
H0431	H. Kidney Medulla, re-excision	Kidney medulla	Kidney			pBluescript
H0433	Human Umbilical Vein Endothelial cells, frac B,	HUVE Cells	Umbilical vein	Cell Line		pBluescript

	re-excision					
H0434	Human Brain, striatum, re-excision	Human Brain, Striatum				pBluescript
H0435	Ovarian Tumor 10-3-95	Ovarian Tumor, OV350721	Ovary			pCMVSport 2.0
H0436	Resting T-Cell Library,II	T-Cells	Blood	Cell Line		pSport1
H0437	H Umbilical Vein Endothelial Cells, frac A, re-excision	HUVE Cells	Umbilical vein	Cell Line		Lambda ZAP II
H0438	H. Whole Brain #2, re-excision	Human Whole Brain #2				ZAP Express
H0441	H. Kidney Cortex, subtracted	Kidney cortex	Kidney			pBluescript
H0442	H. Striatum Depression, subt II	Human Brain, Striatum Depression	Brain			pBluescript
H0445	Spleen, Chronic lymphocytic leukemia	Human Spleen, CLL	Spleen		disease	pSport1
H0457	Human Eosinophils	Human Eosinophils				pSport1
H0459	CD34+cells, II, FRACTION 2	CD34 positive cells				pCMVSport 2.0
H0461	H. Kidney Medulla, subtracted	Kidney medulla	Kidney			pBluescript
H0477	Human Tonsil, Lib 3	Human Tonsil	Tonsil			pSport1
H0478	Salivary Gland, Lib 2	Human Salivary Gland	Salivary gland			pSport1
H0483	Breast Cancer cell line, MDA 36	Breast Cancer Cell line, MDA 36				pSport1
H0484	Breast Cancer Cell line, angiogenic	Breast Cancer Cell line, Angiogenic, 36T3				pSport1
H0485	Hodgkin"s Lymphoma I	Hodgkin"s			disease	pCMVSport

		Lymphoma I				2.0
H0486	Hodgkin"s Lymphoma II	Hodgkin"s Lymphoma II			disease	pCMVSport 2.0
H0488	Human Tonsils, Lib 2	Human Tonsils				pCMVSport 2.0
H0489	Crohn"s Disease	Ileum	Intestine		disease	pSport1
H0492	HL-60, RA 4h, Subtracted	HL-60 Cells, RA stimulated for 4H	Blood	Cell Line		Uni-ZAP XR
H0494	Keratinocyte	Keratinocyte				pCMVSport 2.0
H0497	HEL cell line	HEL cell line		HEL 92.1.7		pSport1
H0505	Human Astrocyte	Human Astrocyte				pSport1
H0506	Ulcerative Colitis	Colon	Colon			pSport1
H0509	Liver, Hepatoma	Human Liver, Hepatoma, patient 8	Liver		disease	pCMVSport 3.0
H0510	Human Liver, normal	Human Liver, normal, Patient # 8	Liver			pCMVSport 3.0
H0512	Keratinocyte, lib 3	Keratinocyte				pCMVSport 2.0
H0518	pBMC stimulated w/ poly I/C	pBMC stimulated with poly I/C				pCMVSport 3.0
H0519	NTERA2, control	NTERA2, Teratocarcinoma cell line				pCMVSport 3.0
H0520	NTERA2 + retinoic acid, 14 days	NTERA2, Teratocarcinoma cell line				pSport1
H0521	Primary Dendritic Cells, lib 1	Primary Dendritic cells				pCMVSport 3.0
H0522	Primary Dendritic cells,frac 2	Primary Dendritic cells				pCMVSport 3.0

H0529	Myoloid Progenitor Cell Line	TF-1 Cell Line; Myoloid progenitor cell line				pCMVSport 3.0
H0539	Pancreas Islet Cell Tumor	Pancreas Islet Cell Tumour	Pancreas		disease	pSport1
H0540	Skin, burned	Skin, leg burned	Skin			pSport1
H0542	T Cell helper I	Helper T cell				pCMVSport 3.0
H0543	T cell helper II	Helper T cell				pCMVSport 3.0
H0544	Human endometrial stromal cells	Human endometrial stromal cells				pCMVSport 3.0
H0545	Human endometrial stromal cells-treated with progesterone	Human endometrial stromal cells-treated with proge				pCMVSport 3.0
H0546	Human endometrial stromal cells-treated with estradiol	Human endometrial stromal cells-treated with estra				pCMVSport 3.0
H0547	NTERA2 teratocarcinoma cell line+retinoic acid (14 days)	NTERA2, Teratocarcinoma cell line				pSport1
H0549	H. Epididiymus, caput & corpus	Human Epididiymus, caput and corpus				Uni-ZAP XR
H0550	H. Epididiymus, cauda	Human Epididiymus, cauda				Uni-ZAP XR
H0551	Human Thymus Stromal Cells	Human Thymus Stromal Cells				pCMVSport 3.0
H0553	Human Placenta	Human Placenta				pCMVSport 3.0
H0555	Rejected Kidney, lib 4	Human Rejected	Kidney		disease	pCMVSport

		Kidney				3.0
H0556	Activated T-cell(12h)/Thiouridine-re-excision	T-Cells	Blood	Cell Line		Uni-ZAP XR
H0559	HL-60, PMA 4H, re-excision	HL-60 Cells, PMA stimulated 4H	Blood	Cell Line		Uni-ZAP XR
H0560	KMH2	KMH2				pCMVSport 3.0
H0561	L428	L428				pCMVSport 3.0
H0567	Human Fetal Brain, normalized A5002F	Human Fetal Brain				pCMVSport 2.0
H0569	Human Fetal Brain, normalized CO	Human Fetal Brain				pCMVSport 2.0
H0570	Human Fetal Brain, normalized C500H	Human Fetal Brain				pCMVSport 2.0
H0572	Human Fetal Brain, normalized AC5002	Human Fetal Brain				pCMVSport 2.0
H0574	Hepatocellular Tumor; re-excision	Hepatocellular Tumor	Liver		disease	Lambda ZAP II
H0575	Human Adult Pulmonary;re-excision	Human Adult Pulmonary	Lung			Uni-ZAP XR
H0580	Dendritic cells, pooled	Pooled dendritic cells				pCMVSport 3.0
H0581	Human Bone Marrow, treated	Human Bone Marrow	Bone Marrow			pCMVSport 3.0
H0583	B Cell lymphoma	B Cell Lymphoma	B Cell		disease	pCMVSport 3.0
H0586	Healing groin wound, 6.5 hours post incision	healing groin wound, 6.5 hours post incision - 2/	groin		disease	pCMVSport 3.0

H0587	Healing groin wound; 7.5 hours post incision	Groin-2/19/97	groin		disease	pCMVSport 3.0
H0589	CD34 positive cells (cord blood),re-ex	CD34 Positive Cells	Cord Blood			ZAP Express
H0590	Human adult small intestine,re-excision	Human Adult Small Intestine	Small Int.			Uni-ZAP XR
H0591	Human T-cell lymphoma;re-excision	T-Cell Lymphoma	T-Cell		disease	Uni-ZAP XR
H0592	Healing groin wound - zero hr post-incision (control)	HGS wound healing project; abdomen			disease	pCMVSport 3.0
H0593	Olfactory epithelium;nasalcavity	Olfactory epithelium from roof of left nasal cacit				pCMVSport 3.0
H0594	Human Lung Cancer;re-excision	Human Lung Cancer	Lung		disease	Lambda ZAP II
H0595	Stomach cancer (human);re-excision	Stomach Cancer - 5383A (human)			disease	Uni-ZAP XR
H0596	Human Colon Cancer;re-excision	Human Colon Cancer	Colon			Lambda ZAP II
H0597	Human Colon; re-excision	Human Colon				Lambda ZAP II
H0598	Human Stomach;re-excision	Human Stomach	Stomach			Uni-ZAP XR
H0599	Human Adult Heart;re-excision	Human Adult Heart	Heart			Uni-ZAP XR
H0600	Healing Abdomen wound;70&90 min post incision	Abdomen			disease	pCMVSport 3.0
H0601	Healing Abdomen Wound;15 days post	Abdomen			disease	pCMVSport 3.0

	incision					
H0604	Human Pituitary, re-excision	Human Pituitary				pBluescript
H0606	Human Primary Breast Cancer;re-excision	Human Primary Breast Cancer	Breast		disease	Uni-ZAP XR
H0608	H. Leukocytes, control	H.Leukocytes				pCMVSport 1
H0610	H. Leukocytes, normalized cot 5A	H.Leukocytes				pCMVSport 1
H0613	H.Leukocytes, normalized cot 5B	H.Leukocytes				pCMVSport 1
H0615	Human Ovarian Cancer Reexcision	Ovarian Cancer	Ovary		disease	Uni-ZAP XR
H0616	Human Testes, Reexcision	Human Testes	Testis			Uni-ZAP XR
H0617	Human Primary Breast Cancer Reexcision	Human Primary Breast Cancer	Breast		disease	Uni-ZAP XR
H0618	Human Adult Testes, Large Inserts, Reexcision	Human Adult Testis	Testis			Uni-ZAP XR
H0619	Fetal Heart	Human Fetal Heart	Heart			Uni-ZAP XR
H0620	Human Fetal Kidney; Reexcision	Human Fetal Kidney	Kidney			Uni-ZAP XR
H0622	Human Pancreas Tumor; Reexcision	Human Pancreas Tumor	Pancreas		disease	Uni-ZAP XR
H0623	Human Umbilical Vein; Reexcision	Human Umbilical Vein Endothelial Cells	Umbilical vein			Uni-ZAP XR
H0624	12 Week Early Stage Human II; Reexcision	Twelve Week Old Early Stage Human	Embryo			Uni-ZAP XR
H0625	Ku 812F Basophils Line	Ku 812F Basophils				pSport1
H0628	Human Pre-Differentiated Adipocytes	Human Pre-Differentiated Adipocytes				Uni-ZAP XR

H0631	Saos2, Dexamethosome Treated	Saos2 Cell Line; Dexamethosome Treated				pSport1
H0632	Hepatocellular Tumor;re-excision	Hepatocellular Tumor	Liver			Lambda ZAP II
H0634	Human Testes Tumor, re-excision	Human Testes Tumor	Testis		disease	Uni-ZAP XR
H0635	Human Activated T-Cells, re-excision	Activated T-Cells	Blood	Cell Line		Uni-ZAP XR
H0636	Chondrocytes	Chondrocytes				pSport1
H0637	Dendritic Cells From CD34 Cells	Dentritic cells from CD34 cells				pSport1
H0638	CD40 activated monocyte dendridic cells	CD40 activated monocyte dendridic cells				pSport1
H0642	Hep G2 Cells, lambda library	Hep G2 Cells				Other
H0644	Human Placenta (re-excision)	Human Placenta	Placenta			Uni-ZAP XR
H0645	Fetal Heart, re-excision	Human Fetal Heart	Heart			Uni-ZAP XR
H0646	Lung, Cancer (4005313 A3): Invasive Poorly Differentiated Lung Adenocarcinoma,	Metastatic squamous cell lung carcinoma, poorly di				pSport1
H0647	Lung, Cancer (4005163 B7): Invasive, Poorly Diff. Adenocarcinoma, Metastatic	Invasive poorly differentiated lung adenocarcinoma			disease	pSport1
H0648	Ovary, Cancer: (4004562 B6) Papillary Serous Cystic Neoplasm, Low	Papillary Cstic neoplasm of low malignant potentia			disease	pSport1

	Malignant Pot					
H0649	Lung, Normal: (4005313 B1)	Normal Lung				pSport1
H0650	B-Cells	B-Cells				pCMVSport 3.0
H0651	Ovary, Normal: (9805C040R)	Normal Ovary				pSport1
H0652	Lung, Normal: (4005313 B1)	Normal Lung				pSport1
H0656	B-cells (unstimulated)	B-cells (unstimulated)				pSport1
H0657	B-cells (stimulated)	B-cells (stimulated)				pSport1
H0658	Ovary, Cancer (9809C332): Poorly differentiated adenocarcinoma	9809C332- Poorly differentiate	Ovary & Fallopian Tubes		disease	pSport1
H0659	Ovary, Cancer (15395A1F): Grade II Papillary Carcinoma	Grade II Papillary Carcinoma, Ovary	Ovary		disease	pSport1
H0660	Ovary, Cancer: (15799A1F) Poorly differentiated carcinoma	Poorly differentiated carcinoma, ovary			disease	pSport1
H0661	Breast, Cancer: (4004943 A5)	Breast cancer			disease	pSport1
H0662	Breast, Normal: (4005522B2)	Normal Breast - #4005522(B2)	Breast			pSport1
H0663	Breast, Cancer: (4005522 A2)	Breast Cancer - #4005522(A2)	Breast		disease	pSport1
H0665	Stromal cells 3.88	Stromal cells 3.88				pSport1
H0667	Stromal cells(HBM3.18)	Stromal cell(HBM 3.18)				pSport1

H0668	stromal cell clone 2.5	stromal cell clone 2.5				pSport1
H0670	Ovary, Cancer(4004650 A3): Well-Differentiated Micropapillary Serous Carcinoma	Ovarian Cancer - 4004650A3				pSport1
H0671	Breast, Cancer: (9802C02OE)	Breast Cancer-Sample # 9802C02OE				pSport1
H0672	Ovary, Cancer: (4004576 A8)	Ovarian Cancer(4004576A8)	Ovary			pSport1
H0673	Human Prostate Cancer, Stage B2; re-excision	Human Prostate Cancer, stage B2	Prostate			Uni-ZAP XR
H0674	Human Prostate Cancer, Stage C; re-excission	Human Prostate Cancer, stage C	Prostate			Uni-ZAP XR
H0677	TNFR degenerate oligo	B-Cells				PCRII
H0682	Serous Papillary Adenocarcinoma	serous papillary adenocarcinoma (9606G304SPA3B)				pCMVSport 3.0
H0684	Serous Papillary Adenocarcinoma	Ovarian Cancer-9810G606	Ovaries			pCMVSport 3.0
H0685	Adenocarcinoma of Ovary, Human Cell Line, # OVCAR-3	Adenocarcinoma of Ovary, Human Cell Line, # OVCAR-				pCMVSport 3.0
H0686	Adenocarcinoma of Ovary, Human Cell Line	Adenocarcinoma of Ovary, Human Cell Line, # SW-626				pCMVSport 3.0
H0687	Human normal ovary(#9610G215)	Human normal ovary(#9610G215)	Ovary			pCMVSport 3.0
H0688	Human Ovarian Cancer(#9807G017)	Human Ovarian cancer(#9807G017),				pCMVSport 3.0

		mRNA from Maura Ru				
H0689	Ovarian Cancer	Ovarian Cancer, #9806G019				pCMVSport 3.0
H0690	Ovarian Cancer, # 9702G001	Ovarian Cancer, #9702G001				pCMVSport 3.0
H0692	BLyS Receptor from Expression Cloning	B Cell Lymphoma	B Cell			pCMVSport 3.0
H0694	Prostate gland adenocarcinoma	Prostate gland, adenocarcinoma, mod/diff, gleason	prostate gland			pCMVSport 3.0
S0001	Brain frontal cortex	Brain frontal cortex	Brain			Lambda ZAP II
S0002	Monocyte activated	Monocyte-activated	blood	Cell Line		Uni-ZAP XR
S0003	Human Osteoclastoma	Osteoclastoma	bone		disease	Uni-ZAP XR
S0006	Neuroblastoma	Human Neural Blastoma			disease	pCDNA
S0007	Early Stage Human Brain	Human Fetal Brain				Uni-ZAP XR
S0010	Human Amygdala	Amygdala				Uni-ZAP XR
S0011	STROMAL - OSTEOCLASTOMA	Osteoclastoma	bone		disease	Uni-ZAP XR
S0013	Prostate	Prostate	prostate			Uni-ZAP XR
S0022	Human Osteoclastoma Stromal Cells - unamplified	Osteoclastoma Stromal Cells				Uni-ZAP XR
S0026	Stromal cell TF274	stromal cell	Bone marrow	Cell Line		Uni-ZAP XR
S0027	Smooth muscle, serum treated	Smooth muscle	Pulmanary artery	Cell Line		Uni-ZAP XR
S0028	Smooth muscle,control	Smooth muscle	Pulmanary artery	Cell Line		Uni-ZAP XR

S0031	Spinal cord	Spinal cord	spinal cord			Uni-ZAP XR
S0035	Brain medulla oblongata	Brain medulla oblongata	Brain			Uni-ZAP XR
S0036	Human Substantia Nigra	Human Substantia Nigra				Uni-ZAP XR
S0037	Smooth muscle, IL1b induced	Smooth muscle	Pulmanary artery	Cell Line		Uni-ZAP XR
S0038	Human Whole Brain #2 - Oligo dT > 1.5Kb	Human Whole Brain #2				ZAP Express
S0040	Adipocytes	Human Adipocytes from Osteoclastoma				Uni-ZAP XR
S0044	Prostate BPH	prostate BPH	Prostate		disease	Uni-ZAP XR
S0045	Endothelial cells-control	Endothelial cell	endothelial cell-lung	Cell Line		Uni-ZAP XR
S0046	Endothelial-induced	Endothelial cell	endothelial cell-lung	Cell Line		Uni-ZAP XR
S0049	Human Brain, Striatum	Human Brain, Striatum				Uni-ZAP XR
S0050	Human Frontal Cortex, Schizophrenia	Human Frontal Cortex, Schizophrenia			disease	Uni-ZAP XR
S0051	Human Hypothalmus,Schizophrenia	Human Hypothalamus, Schizophrenia			disease	Uni-ZAP XR
S0052	neutrophils control	human neutrophils	blood	Cell Line		Uni-ZAP XR
S0053	Neutrophils IL-1 and LPS induced	human neutrophil induced	blood	Cell Line		Uni-ZAP XR
S0106	STRIATUM		BRAIN		disease	Uni-ZAP XR

	DEPRESSION					
S0114	Anergic T-cell	Anergic T-cell		Cell Line		Uni-ZAP XR
S0116	Bone marrow	Bone marrow	Bone marrow			Uni-ZAP XR
S0126	Osteoblasts	Osteoblasts	Knee	Cell Line		Uni-ZAP XR
S0132	Epithelial-TNFa and INF induced	Airway Epithelial				Uni-ZAP XR
S0134	Apoptotic T-cell	apoptotic cells		Cell Line		Uni-ZAP XR
S0136	PERM TF274	stromal cell	Bone marrow	Cell Line		Lambda ZAP II
S0142	Macrophage-oxLDL	macrophage-oxidized LDL treated	blood	Cell Line		Uni-ZAP XR
S0144	Macrophage (GM-CSF treated)	Macrophage (GM-CSF treated)				Uni-ZAP XR
S0150	LNCAP prostate cell line	LNCAP Cell Line	Prostate	Cell Line		Uni-ZAP XR
S0152	PC3 Prostate cell line	PC3 prostate cell line				Uni-ZAP XR
S0180	Bone Marrow Stroma, TNF&LPS ind	Bone Marrow Stroma, TNF & LPS induced			disease	Uni-ZAP XR
S0182	Human B Cell 8866	Human B- Cell 8866				Uni-ZAP XR
S0190	Prostate BPH,Lib 2, subtracted	Human Prostate BPH				pSport1
S0192	Synovial Fibroblasts (control)	Synovial Fibroblasts				pSport1
S0194	Synovial hypoxia	Synovial Fibroblasts				pSport1
S0196	Synovial IL-1/TNF stimulated	Synovial Fibroblasts				pSport1
S0206	Smooth Muscle- HASTE normalized	Smooth muscle	Pulmanary artery	Cell Line		pBluescript

S0210	Messangial cell, frac 2	Messangial cell				pSport1
S0212	Bone Marrow Stromal Cell, untreated	Bone Marrow Stromal Cell,untreated				pSport1
S0214	Human Osteoclastoma, re-excision	Osteoclastoma	bone		disease	Uni-ZAP XR
S0216	Neutrophils IL-1 and LPS induced	human neutrophil induced	blood	Cell Line		Uni-ZAP XR
S0218	Apoptotic T-cell, re-excision	apoptotic cells		Cell Line		Uni-ZAP XR
S0222	H. Frontal cortex,epileptic;re-excision	H. Brain, Frontal Cortex, Epileptic	Brain		disease	Uni-ZAP XR
S0242	Synovial Fibroblasts (Il1/TNF), subt	Synovial Fibroblasts				pSport1
S0250	Human Osteoblasts II	Human Osteoblasts	Femur		disease	pCMVSport 2.0
S0260	Spinal Cord, re-excision	Spinal cord	spinal cord			Uni-ZAP XR
S0276	Synovial hypoxia-RSF subtracted	Synovial fobroblasts (rheumatoid)	Synovial tissue			pSport1
S0278	H Macrophage (GM-CSF treated), re-excision	Macrophage (GM-CSF treated)				Uni-ZAP XR
S0280	Human Adipose Tissue, re-excision	Human Adipose Tissue				Uni-ZAP XR
S0282	Brain Frontal Cortex, re-excision	Brain frontal cortex	Brain			Lambda ZAP II
S0300	Frontal lobe,dementia;re-excision	Frontal Lobe dementia/Alzheimer's	Brain			Uni-ZAP XR
S0308	Spleen/normal	Spleen normal				pSport1

S0314	Human osteoarthritis;fraction I	Human osteoarthritic cartilage			disease	pSport1
S0328	Palate carcinoma	Palate carcinoma	Uvula		disease	pSport1
S0330	Palate normal	Palate normal	Uvula			pSport1
S0332	Pharynx carcinoma	Pharynx carcinoma	Hypopharynx			pSport1
S0342	Adipocytes;re-excision	Human Adipocytes from Osteoclastoma				Uni-ZAP XR
S0344	Macrophage-oxLDL; re-excision	macrophage-oxidized LDL treated	blood	Cell Line		Uni-ZAP XR
S0346	Human Amygdala;re-excision	Amygdala				Uni-ZAP XR
S0352	Larynx Carcinoma	Larynx carcinoma			disease	pSport1
S0354	Colon Normal II	Colon Normal	Colon			pSport1
S0356	Colon Carcinoma	Colon Carcinoma	Colon		disease	pSport1
S0358	Colon Normal III	Colon Normal	Colon			pSport1
S0360	Colon Tumor II	Colon Tumor	Colon		disease	pSport1
S0364	Human Quadriceps	Quadriceps muscle				pSport1
S0366	Human Soleus	Soleus Muscle				pSport1
S0374	Normal colon	Normal colon				pSport1
S0376	Colon Tumor	Colon Tumor			disease	pSport1
S0378	Pancreas normal PCA4 No	Pancreas Normal PCA4 No				pSport1
S0380	Pancreas Tumor PCA4 Tu	Pancreas Tumor PCA4 Tu			disease	pSport1
S0382	Larynx carcinoma IV	Larynx carcinoma			disease	pSport1
S0384	Tongue carcinoma	Tongue carcinoma			disease	pSport1
S0386	Human Whole Brain, re-excision	Whole brain	Brain			ZAP Express

S0388	Human Hypothalamus,schizophrenia, re-excision	Human Hypothalamus, Schizophrenia			disease	Uni-ZAP XR
S0390	Smooth muscle, control; re-excision	Smooth muscle	Pulmanary artery	Cell Line		Uni-ZAP XR
S0404	Rectum normal	Rectum, normal				pSport1
S0406	Rectum tumour	Rectum tumour				pSport1
S0408	Colon, normal	Colon, normal				pSport1
S0410	Colon, tumour	Colon, tumour				pSport1
S0412	Temporal cortex-Alzheizmer; subtracted	Temporal cortex, alzheimer			disease	Other
S0418	CHME Cell Line;treated 5 hrs	CHME Cell Line; treated				pCMVSport 3.0
S0420	CHME Cell Line,untreated	CHME Cell line, untreatetd				pSport1
S0422	Mo7e Cell Line GM-CSF treated (1ng/ml)	Mo7e Cell Line GM-CSF treated (1ng/ml)				pCMVSport 3.0
S0424	TF-1 Cell Line GM-CSF Treated	TF-1 Cell Line GM-CSF Treated				pSport1
S0426	Monocyte activated; re-excision	Monocyte-activated	blood	Cell Line		Uni-ZAP XR
S0428	Neutrophils control; re-excision	human neutrophils	blood	Cell Line		Uni-ZAP XR
S0434	Stomach Normal	Stomach Normal			disease	pSport1
S0436	Stomach Tumour	Stomach Tumour			disease	pSport1
S0438	Liver Normal Met5No	Liver Normal Met5No				pSport1
S0440	Liver Tumour Met 5 Tu	Liver Tumour				pSport1
S0442	Colon Normal	Colon Normal				pSport1
S0444	Colon Tumor	Colon Tumour			disease	pSport1

S0452	Thymus	Thymus				pSport1
S0462	Thyroid Thyroiditis	Thyroid Thyroiditis				pSport1
S0472	Lung Mesothelium	PYBT				pSport1
S0474	Human blood platelets	Platelets	Blood platelets			Other
S3012	Smooth Muscle Serum Treated, Norm	Smooth muscle	Pulmanary artery	Cell Line		pBluescript
S3014	Smooth muscle, serum induced,re-exc	Smooth muscle	Pulmanary artery	Cell Line		pBluescript
S6022	H. Adipose Tissue	Human Adipose Tissue				Uni-ZAP XR
S6024	Alzheimers, spongy change	Alzheimer"s/Spongy change	Brain		disease	Uni-ZAP XR
S6026	Frontal Lobe, Dementia	Frontal Lobe dementia/Alzheimer''s	Brain			Uni-ZAP XR
S6028	Human Manic Depression Tissue	Human Manic depression tissue	Brain		disease	Uni-ZAP XR
T0002	Activated T-cells	Activated T-Cell, PBL fraction	Blood	Cell Line		pBluescript SK-
T0003	Human Fetal Lung	Human Fetal Lung				pBluescript SK-
T0006	Human Pineal Gland	Human Pinneal Gland				pBluescript SK-
T0010	Human Infant Brain	Human Infant Brain				Other
T0023	Human Pancreatic Carcinoma	Human Pancreatic Carcinoma			disease	pBluescript SK-
T0039	HSA 172 Cells	Human HSA172 cell line				pBluescript SK-
T0040	HSC172 cells	SA172 Cells				pBluescript SK-

T0041	Jurkat T-cell G1 phase	Jurkat T-cell				pBluescript SK-
T0042	Jurkat T-Cell, S phase	Jurkat T-Cell Line				pBluescript SK-
T0048	Human Aortic Endothelium	Human Aortic Endothilium				pBluescript SK-
T0049	Aorta endothelial cells + TNF-a	Aorta endothelial cells				pBluescript SK-
T0060	Human White Adipose	Human White Fat				pBluescript SK-
T0082	Human Adult Retina	Human Adult Retina				pBluescript SK-
T0109	Human (HCC) cell line liver (mouse) metastasis, remake					pBluescript SK-
T0110	Human colon carcinoma (HCC) cell line, remake					pBluescript SK-
T0114	Human (Caco-2) cell line, adenocarcinoma, colon, remake					pBluescript SK-
T0115	Human Colon Carcinoma (HCC) cell line					pBluescript SK-
L0002	Atrium cDNA library Human heart					
L0005	Clontech human aorta polyA+ mRNA (#6572)					
L0021	Human adult (K.Okubo)					
L0022	Human adult lung 3" directed MboI cDNA					
L0040	Human colon mucosa					
L0041	Human epidermal					

	keratinocyte					
L0055	Human promyelocyte					
L0065	Liver HepG2 cell line.					
L0105	Human aorta polyA+ (TFujiwara)	aorta				
L0143	Human placenta polyA+ (TFujiwara)	placenta				
L0157	Human fetal brain (TFujiwara)		brain			
L0163	Human heart cDNA (YNakamura)		heart			
L0251	Homo sapiens laryngeal cancer	laryngeal cancer				
L0351	Infant brain, Bento Soares					BA, M13-derived
L0352	Normalized infant brain, Bento Soares					BA, M13-derived
L0361	Stratagene ovary (#937217)		ovary			Bluescript SK
L0362	Stratagene ovarian cancer (#937219)					Bluescript SK-
L0363	NCI_CGAP_GC2	germ cell tumor				Bluescript SK-
L0364	NCI_CGAP_GC5	germ cell tumor				Bluescript SK-
L0366	Stratagene schizo brain S11	schizophrenic brain S-11 frontal lobe				Bluescript SK-
L0369	NCI_CGAP_AA1	adrenal adenoma	adrenal gland			Bluescript SK-
L0371	NCI_CGAP_Br3	breast tumor	breast			Bluescript SK-
L0372	NCI_CGAP_Co12	colon tumor	colon			Bluescript SK-
L0373	NCI_CGAP_Co11	tumor	colon			Bluescript SK-
L0374	NCI_CGAP_Co2	tumor	colon			Bluescript SK-

L0375	NCI_CGAP_Kid6	kidney tumor	kidney			Bluescript SK-
L0378	NCI_CGAP_Lu1	lung tumor	lung			Bluescript SK-
L0379	NCI_CGAP_Lym3	lymphoma	lymph node			Bluescript SK-
L0381	NCI_CGAP_HN4	squamous cell carcinoma	pharynx			Bluescript SK-
L0382	NCI_CGAP_Pr25	epithelium (cell line)	prostate			Bluescript SK-
L0383	NCI_CGAP_Pr24	invasive tumor (cell line)	prostate			Bluescript SK-
L0387	NCI_CGAP_GCB0	germinal center B-cells	tonsil			Bluescript SK-
L0388	NCI_CGAP_HN6	normal gingiva (cell line from immortalized kerati				Bluescript SK-
L0411	1-NIB					Lafmid BA
L0427	b4HB3MA-FT20%-Biotin					Lafmid BA
L0435	Infant brain, LLNL array of Dr. M. Soares 1NIB					lafmid BA
L0438	normalized infant brain cDNA	total brain	brain			lafmid BA
L0439	Soares infant brain 1NIB		whole brain			Lafmid BA
L0455	Human retina cDNA randomly primed sublibrary	retina	eye			lambda gt10
L0456	Human retina cDNA Tsp509I-cleaved sublibrary	retina	eye			lambda gt10
L0471	Human fetal heart, Lambda ZAP Express					Lambda ZAP Express
L0475	KG1-a Lambda Zap			KG1-a		Lambda Zap

	Express cDNA library					Express (Stratagene)
L0483	Human pancreatic islet					Lambda ZAPII
L0485	STRATAGENE Human skeletal muscle cDNA library, cat. #936215.	skeletal muscle	leg muscle			Lambda ZAPII
L0499	NCI_CGAP_HSC2	stem cell 34+/38+	bone marrow			pAMP1
L0500	NCI_CGAP_Brn20	oligodendroglioma	brain			pAMP1
L0509	NCI_CGAP_Lu26	invasive adenocarcinoma	lung			pAMP1
L0512	NCI_CGAP_Ov36	borderline ovarian carcinoma	ovary			pAMP1
L0515	NCI_CGAP_Ov32	papillary serous carcinoma	ovary			pAMP1
L0517	NCI_CGAP_Pr1					pAMP10
L0518	NCI_CGAP_Pr2					pAMP10
L0519	NCI_CGAP_Pr3					pAMP10
L0520	NCI_CGAP_Alv1	alveolar rhabdomyosarcoma				pAMP10
L0521	NCI_CGAP_Ew1	Ewing"s sarcoma				pAMP10
L0526	NCI_CGAP_Pr12	metastatic prostate bone lesion				pAMP10
L0532	NCI_CGAP_Thy1	thyroid				pAMP10
L0540	NCI_CGAP_Pr10	invasive prostate tumor	prostate			pAMP10
L0542	NCI_CGAP_Pr11	normal prostatic epithelial cells	prostate			pAMP10
L0543	NCI_CGAP_Pr9	normal prostatic epithelial cells	prostate			pAMP10

L0547	NCI_CGAP_Pr16	tumor	prostate			pAMP10
L0559	NCI_CGAP_Ov39	papillary serous ovarian metastasis	ovary			pAMP10
L0564	Jia bone marrow stroma	bone marrow stroma				pBluescript
L0565	Normal Human Trabecular Bone Cells	Bone	Hip			pBluescript
L0581	Stratagene liver (#937224)		liver			pBluescript SK
L0588	Stratagene endothelial cell 937223					pBluescript SK-
L0591	Stratagene HeLa cell s3 937216					pBluescript SK-
L0592	Stratagene hNT neuron (#937233)					pBluescript SK-
L0593	Stratagene neuroepithelium (#937231)					pBluescript SK-
L0594	Stratagene neuroepithelium NT2RAMI 937234					pBluescript SK-
L0595	Stratagene NT2 neuronal precursor 937230	neuroepithelial cells	brain			pBluescript SK-
L0596	Stratagene colon (#937204)		colon			pBluescript SK-
L0597	Stratagene corneal stroma (#937222)		cornea			pBluescript SK-
L0598	Morton Fetal Cochlea	cochlea	ear			pBluescript SK-
L0599	Stratagene lung (#937210)		lung			pBluescript SK-
L0601	Stratagene pancreas		pancreas			pBluescript

	(#937208)					SK-
L0603	Stratagene placenta (#937225)		placenta			pBluescript SK-
L0604	Stratagene muscle 937209	muscle	skeletal muscle			pBluescript SK-
L0605	Stratagene fetal spleen (#937205)	fetal spleen	spleen			pBluescript SK-
L0608	Stratagene lung carcinoma 937218	lung carcinoma	lung	NCI-H69		pBluescript SK-
L0622	HM1					pcDNAII (Invitrogen)
L0623	HM3	pectoral muscle (after mastectomy)				pcDNAII (Invitrogen)
L0627	NCI_CGAP_Co1	bulk tumor	colon			pCMV-SPORT2
L0629	NCI_CGAP_Mel3	metastatic melanoma to bowel	bowel (skin primary)			pCMV-SPORT4
L0630	NCI_CGAP_CNS1	substantia nigra	brain			pCMV-SPORT4
L0634	NCI_CGAP_Ov8	serous adenocarcinoma	ovary			pCMV-SPORT4
L0637	NCI_CGAP_Brn53	three pooled meningiomas	brain			pCMV-SPORT6
L0638	NCI_CGAP_Brn35	tumor, 5 pooled (see description)	brain			pCMV-SPORT6
L0639	NCI_CGAP_Brn52	tumor, 5 pooled (see description)	brain			pCMV-SPORT6
L0640	NCI_CGAP_Br18	four pooled high-grade tumors, including two prima	breast			pCMV-SPORT6

L0641	NCI_CGAP_Co17	juvenile granulosa tumor	colon			pCMV-SPORT6
L0642	NCI_CGAP_Co18	moderately differentiated adenocarcinoma	colon			pCMV-SPORT6
L0643	NCI_CGAP_Co19	moderately differentiated adenocarcinoma	colon			pCMV-SPORT6
L0644	NCI_CGAP_Co20	moderately differentiated adenocarcinoma	colon			pCMV-SPORT6
L0645	NCI_CGAP_Co21	moderately differentiated adenocarcinoma	colon			pCMV-SPORT6
L0646	NCI_CGAP_Co14	moderately-differentiated adenocarcinoma	colon			pCMV-SPORT6
L0647	NCI_CGAP_Sar4	five pooled sarcomas, including myxoid liposarcoma	connective tissue			pCMV-SPORT6
L0648	NCI_CGAP_Eso2	squamous cell carcinoma	esophagus			pCMV-SPORT6
L0649	NCI_CGAP_GU1	2 pooled high-grade transitional cell tumors	genitourinary tract			pCMV-SPORT6
L0650	NCI_CGAP_Kid13	2 pooled Wilms" tumors, one primary and one metast	kidney			pCMV-SPORT6
L0651	NCI_CGAP_Kid8	renal cell tumor	kidney			pCMV-SPORT6
L0653	NCI_CGAP_Lu28	two pooled	lung			pCMV-

		squamous cell carcinomas				SPORT6
L0655	NCI_CGAP_Lym12	lymphoma, follicular mixed small and large cell	lymph node			pCMV-SPORT6
L0657	NCI_CGAP_Ov23	tumor, 5 pooled (see description)	ovary			pCMV-SPORT6
L0659	NCI_CGAP_Pan1	adenocarcinoma	pancreas			pCMV-SPORT6
L0661	NCI_CGAP_Mel15	malignant melanoma, metastatic to lymph node	skin			pCMV-SPORT6
L0662	NCI_CGAP_Gas4	poorly differentiated adenocarcinoma with signet r	stomach			pCMV-SPORT6
L0663	NCI_CGAP_Ut2	moderately-differentiated endometrial adenocarcino	uterus			pCMV-SPORT6
L0664	NCI_CGAP_Ut3	poorly-differentiated endometrial adenocarcinoma,	uterus			pCMV-SPORT6
L0665	NCI_CGAP_Ut4	serous papillary carcinoma, high grade, 2 pooled t	uterus			pCMV-SPORT6
L0666	NCI_CGAP_Ut1	well-differentiated endometrial adenocarcinoma, 7	uterus			pCMV-SPORT6
L0667	NCI_CGAP_CML1	myeloid cells, 18 pooled CML cases,	whole blood			pCMV-SPORT6

		BCR/ABL rearra				
L0697	Testis 1					PGEM 5zf(+)
L0717	Gessler Wilms tumor					pSPORT1
L0731	Soares_pregnant_uterus_ NbHPU		uterus			pT7T3-Pac
L0738	Human colorectal cancer					pT7T3D
L0740	Soares melanocyte 2NbHM	melanocyte				pT7T3D (Pharmacia) with a modified polylinker
L0741	Soares adult brain N2b4HB55Y		brain			pT7T3D (Pharmacia) with a modified polylinker
L0742	Soares adult brain N2b5HB55Y		brain			pT7T3D (Pharmacia) with a modified polylinker
L0743	Soares breast 2NbHBst		breast			pT7T3D (Pharmacia) with a modified polylinker
L0744	Soares breast 3NbHBst		breast			pT7T3D (Pharmacia) with a modified polylinker

L0745	Soares retina N2b4HR	retina	eye			pT7T3D (Pharmacia) with a modified polylinker
L0746	Soares retina N2b5HR	retina	eye			pT7T3D (Pharmacia) with a modified polylinker
L0747	Soares_fetal_heart_NbHH 19W		heart			pT7T3D (Pharmacia) with a modified polylinker
L0748	Soares fetal liver spleen 1NFLS		Liver and Spleen			pT7T3D (Pharmacia) with a modified polylinker
L0749	Soares_fetal_liver_spleen _1NFLS_S1		Liver and Spleen			pT7T3D (Pharmacia) with a modified polylinker
L0750	Soares_fetal_lung_NbHL1 9W		lung			pT7T3D (Pharmacia) with a modified polylinker
L0751	Soares ovary tumor	ovarian tumor	ovary			pT7T3D

	NbHOT					(Pharmacia) with a modified polylinker
L0752	Soares_parathyroid_tumor_NbHPA	parathyroid tumor	parathyroid gland			pT7T3D (Pharmacia) with a modified polylinker
L0754	Soares placenta Nb2HP		placenta			pT7T3D (Pharmacia) with a modified polylinker
L0755	Soares_placenta_8to9weeks_2NbHP8to9W		placenta			pT7T3D (Pharmacia) with a modified polylinker
L0756	Soares_multiple_sclerosis_2NbHMSP	multiple sclerosis lesions				pT7T3D (Pharmacia) with a modified polylinker V_TYPE
L0757	Soares_senescent_fibroblasts_NbHSF	senescent fibroblast				pT7T3D (Pharmacia) with a modified polylinker V_TYPE

L0758	Soares_testis_NHT					pT7T3D-Pac (Pharmacia) with a modified polylinker
L0759	Soares_total_fetus_Nb2HF8_9w					pT7T3D-Pac (Pharmacia) with a modified polylinker
L0761	NCI_CGAP_CLL1	B-cell, chronic lymphotic leukemia				pT7T3D-Pac (Pharmacia) with a modified polylinker
L0762	NCI_CGAP_Br1.1	breast				pT7T3D-Pac (Pharmacia) with a modified polylinker
L0763	NCI_CGAP_Br2	breast				pT7T3D-Pac (Pharmacia) with a modified polylinker
L0764	NCI_CGAP_Co3	colon				pT7T3D-Pac (Pharmacia) with a modified polylinker
L0766	NCI_CGAP_GCB1	germinal center B				pT7T3D-Pac

		cell				(Pharmacia) with a modified polylinker
L0768	NCI_CGAP_GC4	pooled germ cell tumors				pT7T3D-Pac (Pharmacia) with a modified polylinker
L0769	NCI_CGAP_Brn25	anaplastic oligodendroglioma	brain			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0770	NCI_CGAP_Brn23	glioblastoma (pooled)	brain			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0771	NCI_CGAP_Co8	adenocarcinoma	colon			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0772	NCI_CGAP_Co10	colon tumor RER+	colon			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0773	NCI_CGAP_Co9	colon tumor RER+	colon			pT7T3D-Pac (Pharmacia)

						with a modified polylinker
L0774	NCI_CGAP_Kid3		kidney			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0775	NCI_CGAP_Kid5	2 pooled tumors (clear cell type)	kidney			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0776	NCI_CGAP_Lu5	carcinoid	lung			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0777	Soares_NhHMPu_S1	Pooled human melanocyte, fetal heart, and pregnant	mixed (see below)			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0778	Barstead pancreas HPLRB1		pancreas			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0779	Soares_NFL_T_GBC_S1		pooled			pT7T3D-Pac (Pharmacia) with a

						modified polylinker
L0780	Soares_NSF_F8_9W_OT_PA_P_S1		pooled			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0782	NCI_CGAP_Pr21	normal prostate	prostate			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0783	NCI_CGAP_Pr22	normal prostate	prostate			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0785	Barstead spleen HPLRB2		spleen			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0787	NCI_CGAP_Sub1					pT7T3D-Pac (Pharmacia) with a modified polylinker
L0788	NCI_CGAP_Sub2					pT7T3D-Pac (Pharmacia) with a modified

						polylinker
L0789	NCI_CGAP_Sub3					pT7T3D-Pac (Pharmacia) with a modified polylinker
L0790	NCI_CGAP_Sub4					pT7T3D-Pac (Pharmacia) with a modified polylinker
L0791	NCI_CGAP_Sub5					pT7T3D-Pac (Pharmacia) with a modified polylinker
L0792	NCI_CGAP_Sub6					pT7T3D-Pac (Pharmacia) with a modified polylinker
L0793	NCI_CGAP_Sub7					pT7T3D-Pac (Pharmacia) with a modified polylinker
L0794	NCI_CGAP_GC6	pooled germ cell tumors				pT7T3D-Pac (Pharmacia) with a modified polylinker

L0796	NCI_CGAP_Brn50	medulloblastoma	brain			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0800	NCI_CGAP_Co16	colon tumor, RER+	colon			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0803	NCI_CGAP_Kid11		kidney			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0804	NCI_CGAP_Kid12	2 pooled tumors (clear cell type)	kidney			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0805	NCI_CGAP_Lu24	carcinoid	lung			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0806	NCI_CGAP_Lu19	squamous cell carcinoma, poorly differentiated (4	lung			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0807	NCI_CGAP_Ov18	fibrotheoma	ovary			pT7T3D-Pac

						(Pharmacia) with a modified polylinker
L0809	NCI_CGAP_Pr28		prostate			pT7T3D-Pac (Pharmacia) with a modified polylinker
L4500	NCI_CGAP_HN16	moderate to poorly differentiated invasive carcino	mouth			pAMP10
L4501	NCI_CGAP_Sub8					pT7T3D-Pac (Pharmacia) with a modified polylinker
L4559	NCI_CGAP_Thy3	follicular carcinoma	thyroid			pCMV-SPORT6
L4763	NCI_CGAP_HN14	hyperplasia of squamous epithelium	tongue			pAMP10
L5566	NCI_CGAP_Brn70	anaplastic oligodendroglioma	brain			pCMV-SPORT6.ccdb
L5574	NCI_CGAP_HN19	normal epithelium	nasopharynx			pAMP10
L5575	NCI_CGAP_Brn65	glioblastoma without EGFR amplification	brain			pCMV-SPORT6
L5622	NCI_CGAP_Skn3		skin			pCMV-SPORT6

L5623	NCI_CGAP_Skn4	squamous cell carcinoma	skin			pCMV-SPORT6

Table 5

SEQ ID NO: X	Cytologic Band or Chromosome:	OMIM Reference(s):
96	12q12-q14	107777 120140 123829 123940 126337 139350 147570 148040 148041 148043 148070 181430 231550 232800 252940 264700 600194 600231 600536 600808 600956 601284 601769 601928 602116 602153

Table 6

OMIM Reference	Description
107777	Diabetes insipidus, nephrogenic, autosomal recessive, 222000
120140	Achondrogenesis-hypochondrogenesis, type II Kniest dysplasia Osteoarthrosis, precocious SED congenita SMED Strudwick type Stickler syndrome, type I Wagner syndrome, type II
123829	Melanoma
123940	White sponge nevus, 193900
126337	Myxoid liposarcoma
139350	Epidermolytic hyperkeratosis, 113800 Keratoderma, palmoplantar, nonepidermolytic
147570	Interferon, immune, deficiency
148040	Epidermolysis bullosa simplex, Koebner, Dowling-Meara, and Weber-Cockayne types, 131900, 131760, 131800
148041	Pachyonychia congenita, Jadassohn-Lewandowsky type, 167200
148043	Meesmann corneal dystrophy, 122100
148070	Liver disease, susceptibility to, from hepatotoxins or viruses
181430	Scapuloperoneal syndrome, myopathic type
231550	Achalasia-addisonianism-alacrimia syndrome
232800	Glycogen storage disease VII
252940	Sanfilippo syndrome, type D
264700	Pseudo-vitamin D dependency rickets 1
600194	Ichthyosis bullosa of Siemens, 146800
600231	Palmoplantar keratoderma, Bothnia type
600536	Myopathy, congenital
600808	Enuresis, nocturnal, 2
600956	Persistent Mullerian duct syndrome, type II, 261550
601284	Hereditary hemorrhagic telangiectasia-2, 600376
601769	Osteoporosis, involutional Rickets, vitamin D-resistant, 277440
601928	Monilethrix, 158000
602116	Glioma
602153	Monilethrix, 158000

The polypeptides of the invention can be prepared in any suitable manner. Such polypeptides include isolated naturally occurring polypeptides, recombinantly produced polypeptides, synthetically produced polypeptides, or polypeptides produced by a combination of these methods. Means for preparing such polypeptides are well understood in the art.

The polypeptides may be in the form of the secreted protein, including the mature form, or may be a part of a larger protein, such as a fusion protein (see below). It is often advantageous to include an additional amino acid sequence which contains secretory or leader sequences, pro-sequences, sequences which aid in purification , such as multiple histidine residues, or an additional sequence for stability during recombinant production.

The polypeptides of the present invention are preferably provided in an isolated form, and preferably are substantially purified. A recombinantly produced version of a polypeptide, including the secreted polypeptide, can be substantially purified using techniques described herein or otherwise known in the art, such as, for example, by the one-step method described in Smith and Johnson, Gene 67:31-40 (1988). Polypeptides of the invention also can be purified from natural, synthetic or recombinant sources using techniques described herein or otherwise known in the art, such as, for example, antibodies of the invention raised against the secreted protein. The present invention provides a polynucleotide comprising, or alternatively consisting of, the nucleic acid sequence of SEQ ID NO:X, and/or a cDNA contained in ATCC deposit Z. The present invention also provides a polypeptide comprising, or alternatively, consisting of, the polypeptide sequence of SEQ ID NO:Y and/or a polypeptide encoded by the cDNA contained in ATCC deposit Z. Polynucleotides encoding a polypeptide comprising, or alternatively consisting of the polypeptide sequence of SEQ ID NO:Y and/or a polypeptide sequence encoded by the cDNA contained in ATCC deposit Z are also encompassed by the invention.

<u>Signal Sequences</u>

The present invention also encompasses mature forms of the polypeptide having the polypeptide sequence of SEQ ID NO:Y and/or the polypeptide sequence encoded by the cDNA in a deposited clone. Polynucleotides encoding the mature

forms (such as, for example, the polynucleotide sequence in SEQ ID NO:X and/or the polynucleotide sequence contained in the cDNA of a deposited clone) are also encompassed by the invention. According to the signal hypothesis, proteins secreted by mammalian cells have a signal or secretary leader sequence which is cleaved from the mature protein once export of the growing protein chain across the rough endoplasmic reticulum has been initiated. Most mammalian cells and even insect cells cleave secreted proteins with the same specificity. However, in some cases, cleavage of a secreted protein is not entirely uniform, which results in two or more mature species of the protein. Further, it has long been known that cleavage specificity of a secreted protein is ultimately determined by the primary structure of the complete protein, that is, it is inherent in the amino acid sequence of the polypeptide.

Methods for predicting whether a protein has a signal sequence, as well as the cleavage point for that sequence, are available. For instance, the method of McGeoch, Virus Res. 3:271-286 (1985), uses the information from a short N-terminal charged region and a subsequent uncharged region of the complete (uncleaved) protein. The method of von Heinje, Nucleic Acids Res. 14:4683-4690 (1986) uses the information from the residues surrounding the cleavage site, typically residues -13 to +2, where +1 indicates the amino terminus of the secreted protein. The accuracy of predicting the cleavage points of known mammalian secretory proteins for each of these methods is in the range of 75-80%. (von Heinje, supra.) However, the two methods do not always produce the same predicted cleavage point(s) for a given protein.

In the present case, the deduced amino acid sequence of the secreted polypeptide was analyzed by a computer program called SignalP (Henrik Nielsen et al., Protein Engineering 10:1-6 (1997)), which predicts the cellular location of a protein based on the amino acid sequence. As part of this computational prediction of localization, the methods of McGeoch and von Heinje are incorporated. The analysis of the amino acid sequences of the secreted proteins described herein by this program provided the results shown in Table 1A.

As one of ordinary skill would appreciate, however, cleavage sites sometimes vary from organism to organism and cannot be predicted with absolute certainty.

Accordingly, the present invention provides secreted polypeptides having a sequence shown in SEQ ID NO:Y which have an N-terminus beginning within 5 residues (i.e., + or - 5 residues) of the predicted cleavage point. Similarly, it is also recognized that in some cases, cleavage of the signal sequence from a secreted protein is not entirely uniform, resulting in more than one secreted species. These polypeptides, and the polynucleotides encoding such polypeptides, are contemplated by the present invention.

Moreover, the signal sequence identified by the above analysis may not necessarily predict the naturally occurring signal sequence. For example, the naturally occurring signal sequence may be further upstream from the predicted signal sequence. However, it is likely that the predicted signal sequence will be capable of directing the secreted protein to the ER. Nonetheless, the present invention provides the mature protein produced by expression of the polynucleotide sequence of SEQ ID NO:X and/or the polynucleotide sequence contained in the cDNA of a deposited clone, in a mammalian cell (e.g., COS cells, as desribed below). These polypeptides, and the polynucleotides encoding such polypeptides, are contemplated by the present invention.

Polynucleotide and Polypeptide Variants

The present invention is directed to variants of the polynucleotide sequence disclosed in SEQ ID NO:X, the complementary strand thereto, and/or the cDNA sequence contained in a deposited clone.

The present invention also encompasses variants of the polypeptide sequence disclosed in SEQ ID NO:Y and/or encoded by a deposited clone.

"Variant" refers to a polynucleotide or polypeptide differing from the polynucleotide or polypeptide of the present invention, but retaining essential properties thereof. Generally, variants are overall closely similar, and, in many regions, identical to the polynucleotide or polypeptide of the present invention. The present invention is also directed to nucleic acid molecules which comprise, or alternatively consist of, a nucleotide sequence which is at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical to, for example, the nucleotide coding sequence in SEQ ID NO:X or the complementary strand thereto, the nucleotide coding sequence

contained in a deposited cDNA clone or the complementary strand thereto, a nucleotide sequence encoding the polypeptide of SEQ ID NO:Y, a nucleotide sequence encoding the polypeptide encoded by the cDNA contained in a deposited clone, and/or polynucleotide fragments of any of these nucleic acid molecules (e.g., those fragments described herein). Polynucleotides which hybridize to these nucleic acid molecules under stringent hybridization conditions or lower stringency conditions are also encompassed by the invention, as are polypeptides encoded by these polynucleotides.

The present invention is also directed to polypeptides which comprise, or alternatively consist of, an amino acid sequence which is at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% identical to, for example, the polypeptide sequence shown in SEQ ID NO:Y, the polypeptide sequence encoded by the cDNA contained in a deposited clone, and/or polypeptide fragments of any of these polypeptides (e.g., those fragments described herein).

By a nucleic acid having a nucleotide sequence at least, for example, 95% "identical" to a reference nucleotide sequence of the present invention, it is intended that the nucleotide sequence of the nucleic acid is identical to the reference sequence except that the nucleotide sequence may include up to five point mutations per each 100 nucleotides of the reference nucleotide sequence encoding the polypeptide. In other words, to obtain a nucleic acid having a nucleotide sequence at least 95% identical to a reference nucleotide sequence, up to 5% of the nucleotides in the reference sequence may be deleted or substituted with another nucleotide, or a number of nucleotides up to 5% of the total nucleotides in the reference sequence may be inserted into the reference sequence. The query sequence may be an entire sequence shown in Table 1A, the ORF (open reading frame), or any fragment specified as described herein.

As a practical matter, whether any particular nucleic acid molecule or polypeptide is at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical to a nucleotide sequence of the presence invention can be determined conventionally using known computer programs. A preferred method for determining the best overall match between a query sequence (a sequence of the present invention) and a subject sequence, also referred to as a global sequence alignment, can be determined

using the FASTDB computer program based on the algorithm of Brutlag et al. (Comp. App. Biosci. 6:237-245(1990)). In a sequence alignment the query and subject sequences are both DNA sequences. An RNA sequence can be compared by converting U's to T's. The result of said global sequence alignment is in percent identity. Preferred parameters used in a FASTDB alignment of DNA sequences to calculate percent identiy are: Matrix=Unitary, k-tuple=4, Mismatch Penalty=1, Joining Penalty=30, Randomization Group Length=0, Cutoff Score=1, Gap Penalty=5, Gap Size Penalty 0.05, Window Size=500 or the lenght of the subject nucleotide sequence, whichever is shorter.

If the subject sequence is shorter than the query sequence because of 5' or 3' deletions, not because of internal deletions, a manual correction must be made to the results. This is because the FASTDB program does not account for 5' and 3' truncations of the subject sequence when calculating percent identity. For subject sequences truncated at the 5' or 3' ends, relative to the query sequence, the percent identity is corrected by calculating the number of bases of the query sequence that are 5' and 3' of the subject sequence, which are not matched/aligned, as a percent of the total bases of the query sequence. Whether a nucleotide is matched/aligned is determined by results of the FASTDB sequence alignment. This percentage is then subtracted from the percent identity, calculated by the above FASTDB program using the specified parameters, to arrive at a final percent identity score. This corrected score is what is used for the purposes of the present invention. Only bases outside the 5' and 3' bases of the subject sequence, as displayed by the FASTDB alignment, which are not matched/aligned with the query sequence, are calculated for the purposes of manually adjusting the percent identity score.

For example, a 90 base subject sequence is aligned to a 100 base query sequence to determine percent identity. The deletions occur at the 5' end of the subject sequence and therefore, the FASTDB alignment does not show a matched/alignment of the first 10 bases at 5' end. The 10 unpaired bases represent 10% of the sequence (number of bases at the 5' and 3' ends not matched/total number of bases in the query sequence) so 10% is subtracted from the percent identity score calculated by the FASTDB program. If the remaining 90 bases were perfectly matched the final percent identity would be 90%. In another example, a 90 base

subject sequence is compared with a 100 base query sequence. This time the deletions are internal deletions so that there are no bases on the 5' or 3' of the subject sequence which are not matched/aligned with the query. In this case the percent identity calculated by FASTDB is not manually corrected. Once again, only bases 5' and 3' of the subject sequence which are not matched/aligned with the query sequence are manually corrected for. No other manual corrections are to made for the purposes of the present invention.

By a polypeptide having an amino acid sequence at least, for example, 95% "identical" to a query amino acid sequence of the present invention, it is intended that the amino acid sequence of the subject polypeptide is identical to the query sequence except that the subject polypeptide sequence may include up to five amino acid alterations per each 100 amino acids of the query amino acid sequence. In other words, to obtain a polypeptide having an amino acid sequence at least 95% identical to a query amino acid sequence, up to 5% of the amino acid residues in the subject sequence may be inserted, deleted, (indels) or substituted with another amino acid. These alterations of the reference sequence may occur at the amino or carboxy terminal positions of the reference amino acid sequence or anywhere between those terminal positions, interspersed either individually among residues in the reference sequence or in one or more contiguous groups within the reference sequence.

As a practical matter, whether any particular polypeptide is at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical to, for instance, an amino acid sequences shown in Table 1A (SEQ ID NO:Y) or to the amino acid sequence encoded by cDNA contained in a deposited clone can be determined conventionally using known computer programs. A preferred method for determing the best overall match between a query sequence (a sequence of the present invention) and a subject sequence, also referred to as a global sequence alignment, can be determined using the FASTDB computer program based on the algorithm of Brutlag et al. (Comp. App. Biosci. 6:237-245(1990)). In a sequence alignment the query and subject sequences are either both nucleotide sequences or both amino acid sequences. The result of said global sequence alignment is in percent identity. Preferred parameters used in a FASTDB amino acid alignment are: Matrix=PAM 0, k-tuple=2, Mismatch Penalty=1, Joining Penalty=20, Randomization Group Length=0, Cutoff Score=1,

Window Size=sequence length, Gap Penalty=5, Gap Size Penalty=0.05, Window Size=500 or the length of the subject amino acid sequence, whichever is shorter.

If the subject sequence is shorter than the query sequence due to N- or C-terminal deletions, not because of internal deletions, a manual correction must be made to the results. This is because the FASTDB program does not account for N- and C-terminal truncations of the subject sequence when calculating global percent identity. For subject sequences truncated at the N- and C-termini, relative to the query sequence, the percent identity is corrected by calculating the number of residues of the query sequence that are N- and C-terminal of the subject sequence, which are not matched/aligned with a corresponding subject residue, as a percent of the total bases of the query sequence. Whether a residue is matched/aligned is determined by results of the FASTDB sequence alignment. This percentage is then subtracted from the percent identity, calculated by the above FASTDB program using the specified parameters, to arrive at a final percent identity score. This final percent identity score is what is used for the purposes of the present invention. Only residues to the N- and C-termini of the subject sequence, which are not matched/aligned with the query sequence, are considered for the purposes of manually adjusting the percent identity score. That is, only query residue positions outside the farthest N- and C-terminal residues of the subject sequence.

For example, a 90 amino acid residue subject sequence is aligned with a 100 residue query sequence to determine percent identity. The deletion occurs at the N-terminus of the subject sequence and therefore, the FASTDB alignment does not show a matching/alignment of the first 10 residues at the N-terminus. The 10 unpaired residues represent 10% of the sequence (number of residues at the N- and C-termini not matched/total number of residues in the query sequence) so 10% is subtracted from the percent identity score calculated by the FASTDB program. If the remaining 90 residues were perfectly matched the final percent identity would be 90%. In another example, a 90 residue subject sequence is compared with a 100 residue query sequence. This time the deletions are internal deletions so there are no residues at the N- or C-termini of the subject sequence which are not matched/aligned with the query. In this case the percent identity calculated by FASTDB is not manually corrected. Once again, only residue positions outside the N- and C-terminal

ends of the subject sequence, as displayed in the FASTDB alignment, which are not matched/aligned with the query sequnce are manually corrected for. No other manual corrections are to made for the purposes of the present invention.

The variants may contain alterations in the coding regions, non-coding regions, or both. Especially preferred are polynucleotide variants containing alterations which produce silent substitutions, additions, or deletions, but do not alter the properties or activities of the encoded polypeptide. Nucleotide variants produced by silent substitutions due to the degeneracy of the genetic code are preferred. Moreover, variants in which 5-10, 1-5, or 1-2 amino acids are substituted, deleted, or added in any combination are also preferred. Polynucleotide variants can be produced for a variety of reasons, e.g., to optimize codon expression for a particular host (change codons in the human mRNA to those preferred by a bacterial host such as E. coli).

Naturally occurring variants are called "allelic variants," and refer to one of several alternate forms of a gene occupying a given locus on a chromosome of an organism. (Genes II, Lewin, B., ed., John Wiley & Sons, New York (1985).) These allelic variants can vary at either the polynucleotide and/or polypeptide level and are included in the present invention. Alternatively, non-naturally occurring variants may be produced by mutagenesis techniques or by direct synthesis.

Using known methods of protein engineering and recombinant DNA technology, variants may be generated to improve or alter the characteristics of the polypeptides of the present invention. For instance, one or more amino acids can be deleted from the N-terminus or C-terminus of the secreted protein without substantial loss of biological function. The authors of Ron et al., J. Biol. Chem. 268: 2984-2988 (1993), reported variant KGF proteins having heparin binding activity even after deleting 3, 8, or 27 amino-terminal amino acid residues. Similarly, Interferon gamma exhibited up to ten times higher activity after deleting 8-10 amino acid residues from the carboxy terminus of this protein. (Dobeli et al., J. Biotechnology 7:199-216 (1988).)

Moreover, ample evidence demonstrates that variants often retain a biological activity similar to that of the naturally occurring protein. For example, Gayle and coworkers (J. Biol. Chem 268:22105-22111 (1993)) conducted extensive mutational

analysis of human cytokine IL-1a. They used random mutagenesis to generate over 3,500 individual IL-1a mutants that averaged 2.5 amino acid changes per variant over the entire length of the molecule. Multiple mutations were examined at every possible amino acid position. The investigators found that "[m]ost of the molecule could be altered with little effect on either [binding or biological activity]." (See, Abstract.) In fact, only 23 unique amino acid sequences, out of more than 3,500 nucleotide sequences examined, produced a protein that significantly differed in activity from wild-type.

Furthermore, even if deleting one or more amino acids from the N-terminus or C-terminus of a polypeptide results in modification or loss of one or more biological functions, other biological activities may still be retained. For example, the ability of a deletion variant to induce and/or to bind antibodies which recognize the secreted form will likely be retained when less than the majority of the residues of the secreted form are removed from the N-terminus or C-terminus. Whether a particular polypeptide lacking N- or C-terminal residues of a protein retains such immunogenic activities can readily be determined by routine methods described herein and otherwise known in the art.

Thus, the invention further includes polypeptide variants which show substantial biological activity. Such variants include deletions, insertions, inversions, repeats, and substitutions selected according to general rules known in the art so as have little effect on activity. For example, guidance concerning how to make phenotypically silent amino acid substitutions is provided in Bowie et al., Science 247:1306-1310 (1990), wherein the authors indicate that there are two main strategies for studying the tolerance of an amino acid sequence to change.

The first strategy exploits the tolerance of amino acid substitutions by natural selection during the process of evolution. By comparing amino acid sequences in different species, conserved amino acids can be identified. These conserved amino acids are likely important for protein function. In contrast, the amino acid positions where substitutions have been tolerated by natural selection indicates that these positions are not critical for protein function. Thus, positions tolerating amino acid substitution could be modified while still maintaining biological activity of the protein.

The second strategy uses genetic engineering to introduce amino acid changes at specific positions of a cloned gene to identify regions critical for protein function. For example, site directed mutagenesis or alanine-scanning mutagenesis (introduction of single alanine mutations at every residue in the molecule) can be used. (Cunningham and Wells, Science 244:1081-1085 (1989).) The resulting mutant molecules can then be tested for biological activity.

As the authors state, these two strategies have revealed that proteins are surprisingly tolerant of amino acid substitutions. The authors further indicate which amino acid changes are likely to be permissive at certain amino acid positions in the protein. For example, most buried (within the tertiary structure of the protein) amino acid residues require nonpolar side chains, whereas few features of surface side chains are generally conserved. Moreover, tolerated conservative amino acid substitutions involve replacement of the aliphatic or hydrophobic amino acids Ala, Val, Leu and Ile; replacement of the hydroxyl residues Ser and Thr; replacement of the acidic residues Asp and Glu; replacement of the amide residues Asn and Gln, replacement of the basic residues Lys, Arg, and His; replacement of the aromatic residues Phe, Tyr, and Trp, and replacement of the small-sized amino acids Ala, Ser, Thr, Met, and Gly.

Besides conservative amino acid substitution, variants of the present invention include (i) substitutions with one or more of the non-conserved amino acid residues, where the substituted amino acid residues may or may not be one encoded by the genetic code, or (ii) substitution with one or more of amino acid residues having a substituent group, or (iii) fusion of the mature polypeptide with another compound, such as a compound to increase the stability and/or solubility of the polypeptide (for example, polyethylene glycol), or (iv) fusion of the polypeptide with additional amino acids, such as, for example, an IgG Fc fusion region peptide, or leader or secretory sequence, or a sequence facilitating purification or (v) fusion of the polypeptide with another compound, such as albumin (including, but not limited to, recombinant albumin (see, e.g., U.S. Patent No. 5,876,969, issued March 2, 1999, EP Patent 0 413 622, and U.S. Patent No. 5,766,883, issued June 16, 1998, herein incorporated by reference in their entirety)). Such variant polypeptides are deemed to be within the scope of those skilled in the art from the teachings herein.

For example, polypeptide variants containing amino acid substitutions of charged amino acids with other charged or neutral amino acids may produce proteins with improved characteristics, such as less aggregation. Aggregation of pharmaceutical formulations both reduces activity and increases clearance due to the aggregate's immunogenic activity. (Pinckard et al., Clin. Exp. Immunol. 2:331-340 (1967); Robbins et al., Diabetes 36: 838-845 (1987); Cleland et al., Crit. Rev. Therapeutic Drug Carrier Systems 10:307-377 (1993).)

A further embodiment of the invention relates to a polypeptide which comprises the amino acid sequence of the present invention having an amino acid sequence which contains at least one amino acid substitution, but not more than 50 amino acid substitutions, even more preferably, not more than 40 amino acid substitutions, still more preferably, not more than 30 amino acid substitutions, and still even more preferably, not more than 20 amino acid substitutions. Of course, in order of ever-increasing preference, it is highly preferable for a peptide or polypeptide to have an amino acid sequence which comprises the amino acid sequence of the present invention, which contains at least one, but not more than 10, 9, 8, 7, 6, 5, 4, 3, 2 or 1 amino acid substitutions. In specific embodiments, the number of additions, substitutions, and/or deletions in the amino acid sequence of the present invention or fragments thereof (e.g., the mature form and/or other fragments described herein), is 1-5, 5-10, 5-25, 5-50, 10-50 or 50-150, conservative amino acid substitutions are preferable.

Polynucleotide and Polypeptide Fragments

The present invention is also directed to polynucleotide fragments of the polynucleotides of the invention.

In the present invention, a "polynucleotide fragment" refers to a short polynucleotide having a nucleic acid sequence which: is a portion of that contained in a deposited clone, or encoding the polypeptide encoded by the cDNA in a deposited clone; is a portion of that shown in SEQ ID NO:X or the complementary strand thereto, or is a portion of a polynucleotide sequence encoding the polypeptide of SEQ ID NO:Y. The nucleotide fragments of the invention are preferably at least about 15 nt, and more preferably at least about 20 nt, still more preferably at least about 30 nt,

and even more preferably, at least about 40 nt, at least about 50 nt, at least about 75 nt, or at least about 150 nt in length. A fragment "at least 20 nt in length," for example, is intended to include 20 or more contiguous bases from the cDNA sequence contained in a deposited clone or the nucleotide sequence shown in SEQ ID NO:X. In this context "about" includes the particularly recited value, a value larger or smaller by several (5, 4, 3, 2, or 1) nucleotides, at either terminus or at both termini. These nucleotide fragments have uses that include, but are not limited to, as diagnostic probes and primers as discussed herein. Of course, larger fragments (e.g., 50, 150, 500, 600, 2000 nucleotides) are preferred.

Moreover, representative examples of polynucleotide fragments of the invention, include, for example, fragments comprising, or alternatively consisting of, a sequence from about nucleotide number 1-50, 51-100, 101-150, 151-200, 201-250, 251-300, 301-350, 351-400, 401-450, 451-500, 501-550, 551-600, 651-700, 701-750, 751-800, 800-850, 851-900, 901-950, 951-1000, 1001-1050, 1051-1100, 1101-1150, 1151-1200, 1201-1250, 1251-1300, 1301-1350, 1351-1400, 1401-1450, 1451-1500, 1501-1550, 1551-1600, 1601-1650, 1651-1700, 1701-1750, 1751-1800, 1801-1850, 1851-1900, 1901-1950, 1951-2000, or 2001 to the end of SEQ ID NO:X, or the complementary strand thereto, or the cDNA contained in a deposited clone. In this context "about" includes the particularly recited ranges, and ranges larger or smaller by several (5, 4, 3, 2, or 1) nucleotides, at either terminus or at both termini. Preferably, these fragments encode a polypeptide which has biological activity. More preferably, these polynucleotides can be used as probes or primers as discussed herein. Polynucleotides which hybridize to these nucleic acid molecules under stringent hybridization conditions or lower stringency conditions are also encompassed by the invention, as are polypeptides encoded by these polynucleotides.

In the present invention, a "polypeptide fragment" refers to an amino acid sequence which is a portion of that contained in SEQ ID NO:Y or encoded by the cDNA contained in a deposited clone. Protein (polypeptide) fragments may be "free-standing," or comprised within a larger polypeptide of which the fragment forms a part or region, most preferably as a single continuous region. Representative examples of polypeptide fragments of the invention, include, for example, fragments comprising, or alternatively consisting of, from about amino acid number 1-20, 21-40,

41-60, 61-80, 81-100, 102-120, 121-140, 141-160, or 161 to the end of the coding region. Moreover, polypeptide fragments can be about 20, 30, 40, 50, 60, 70, 80, 90, 100, 110, 120, 130, 140, or 150 amino acids in length. In this context "about" includes the particularly recited ranges or values, and ranges or values larger or smaller by several (5, 4, 3, 2, or 1) amino acids, at either extreme or at both extremes. Polynucleotides encoding these polypeptides are also encompassed by the invention.

Preferred polypeptide fragments include the secreted protein as well as the mature form. Further preferred polypeptide fragments include the secreted protein or the mature form having a continuous series of deleted residues from the amino or the carboxy terminus, or both. For example, any number of amino acids, ranging from 1-60, can be deleted from the amino terminus of either the secreted polypeptide or the mature form. Similarly, any number of amino acids, ranging from 1-30, can be deleted from the carboxy terminus of the secreted protein or mature form. Furthermore, any combination of the above amino and carboxy terminus deletions are preferred. Similarly, polynucleotides encoding these polypeptide fragments are also preferred.

Also preferred are polypeptide and polynucleotide fragments characterized by structural or functional domains, such as fragments that comprise alpha-helix and alpha-helix forming regions, beta-sheet and beta-sheet-forming regions, turn and turn-forming regions, coil and coil-forming regions, hydrophilic regions, hydrophobic regions, alpha amphipathic regions, beta amphipathic regions, flexible regions, surface-forming regions, substrate binding region, and high antigenic index regions. Polypeptide fragments of SEQ ID NO:Y falling within conserved domains are specifically contemplated by the present invention. Moreover, polynucleotides encoding these domains are also contemplated.

Other preferred polypeptide fragments are biologically active fragments. Biologically active fragments are those exhibiting activity similar, but not necessarily identical, to an activity of the polypeptide of the present invention. The biological activity of the fragments may include an improved desired activity, or a decreased undesirable activity. Polynucleotides encoding these polypeptide fragments are also encompassed by the invention.

Preferably, the polynucleotide fragments of the invention encode a polypeptide which demonstrates a functional activity. By a polypeptide demonstrating a "functional activity" is meant, a polypeptide capable of displaying one or more known functional activities associated with a full-length (complete) polypeptide of invention protein. Such functional activities include, but are not limited to, biological activity, antigenicity [ability to bind (or compete with a polypeptide of the invention for binding) to an antibody to the polypeptide of the invention], immunogenicity (ability to generate antibody which binds to a polypeptide of the invention), ability to form multimers with polypeptides of the invention, and ability to bind to a receptor or ligand for a polypeptide of the invention.

The functional activity of polypeptides of the invention, and fragments, variants derivatives, and analogs thereof, can be assayed by various methods.

For example, in one embodiment where one is assaying for the ability to bind or compete with full-length polypeptide of the invention for binding to an antibody of the polypeptide of the invention, various immunoassays known in the art can be used, including but not limited to, competitive and non-competitive assay systems using techniques such as radioimmunoassays, ELISA (enzyme linked immunosorbent assay), "sandwich" immunoassays, immunoradiometric assays, gel diffusion precipitation reactions, immunodiffusion assays, in situ immunoassays (using colloidal gold, enzyme or radioisotope labels, for example), western blots, precipitation reactions, agglutination assays (e.g., gel agglutination assays, hemagglutination assays), complement fixation assays, immunofluorescence assays, protein A assays, and immunoelectrophoresis assays, etc. In one embodiment, antibody binding is detected by detecting a label on the primary antibody. In another embodiment, the primary antibody is detected by detecting binding of a secondary antibody or reagent to the primary antibody. In a further embodiment, the secondary antibody is labeled. Many means are known in the art for detecting binding in an immunoassay and are within the scope of the present invention.

In another embodiment, where a ligand for a polypeptide of the invention identified, or the ability of a polypeptide fragment, variant or derivative of the invention to multimerize is being evaluated, binding can be assayed, e.g., by means well-known in the art, such as, for example, reducing and non-reducing gel

chromatography, protein affinity chromatography, and affinity blotting. See generally, Phizicky, E., et al., 1995, Microbiol. Rev. 59:94-123. In another embodiment, physiological correlates of binding of a polypeptide of the invention to its substrates (signal transduction) can be assayed.

In addition, assays described herein (see Examples) and otherwise known in the art may routinely be applied to measure the ability of polypeptides of the invention and fragments, variants derivatives and analogs thereof to elicit related biological activity related to that of the polypeptide of the invention (either in vitro or in vivo). Other methods will be known to the skilled artisan and are within the scope of the invention.

Epitopes and Antibodies

The present invention encompasses polypeptides comprising, or alternatively consisting of, an epitope of the polypeptide having an amino acid sequence of SEQ ID NO:Y, or an epitope of the polypeptide sequence encoded by a polynucleotide sequence contained in ATCC deposit No. Z or encoded by a polynucleotide that hybridizes to the complement of the sequence of SEQ ID NO:X or contained in ATCC deposit No. Z under stringent hybridization conditions or lower stringency hybridization conditions as defined supra. The present invention further encompasses polynucleotide sequences encoding an epitope of a polypeptide sequence of the invention (such as, for example, the sequence disclosed in SEQ ID NO:X), polynucleotide sequences of the complementary strand of a polynucleotide sequence encoding an epitope of the invention, and polynucleotide sequences which hybridize to the complementary strand under stringent hybridization conditions or lower stringency hybridization conditions defined supra.

The term "epitopes," as used herein, refers to portions of a polypeptide having antigenic or immunogenic activity in an animal, preferably a mammal, and most preferably in a human. In a preferred embodiment, the present invention encompasses a polypeptide comprising an epitope, as well as the polynucleotide encoding this polypeptide. An "immunogenic epitope," as used herein, is defined as a portion of a protein that elicits an antibody response in an animal, as determined by any method known in the art, for example, by the methods for generating antibodies

described infra. (See, for example, Geysen et al., Proc. Natl. Acad. Sci. USA 81:3998- 4002 (1983)). The term "antigenic epitope," as used herein, is defined as a portion of a protein to which an antibody can immunospecifically bind its antigen as determined by any method well known in the art, for example, by the immunoassays described herein. Immunospecific binding excludes non-specific binding but does not necessarily exclude cross- reactivity with other antigens. Antigenic epitopes need not necessarily be immunogenic.

Fragments which function as epitopes may be produced by any conventional means. (See, e.g., Houghten, Proc. Natl. Acad. Sci. USA 82:5131-5135 (1985), further described in U.S. Patent No. 4,631,211).

In the present invention, antigenic epitopes preferably contain a sequence of at least 4, at least 5, at least 6, at least 7, more preferably at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 20, at least 25, at least 30, at least 40, at least 50, and, most preferably, between about 15 to about 30 amino acids. Preferred polypeptides comprising immunogenic or antigenic epitopes are at least 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, or 100 amino acid residues in length. Additional non-exclusive preferred antigenic epitopes include the antigenic epitopes disclosed herein, as well as portions thereof. Antigenic epitopes are useful, for example, to raise antibodies, including monoclonal antibodies, that specifically bind the epitope. Preferred antigenic epitopes include the antigenic epitopes disclosed herein, as well as any combination of two, three, four, five or more of these antigenic epitopes. Antigenic epitopes can be used as the target molecules in immunoassays. (See, for instance, Wilson et al., Cell 37:767-778 (1984); Sutcliffe et al., Science 219:660-666 (1983)).

Similarly, immunogenic epitopes can be used, for example, to induce antibodies according to methods well known in the art. (See, for instance, Sutcliffe et al., supra; Wilson et al., supra; Chow et al., Proc. Natl. Acad. Sci. USA 82:910-914; and Bittle et al., J. Gen. Virol. 66:2347-2354 (1985). Preferred immunogenic epitopes include the immunogenic epitopes disclosed herein, as well as any combination of two, three, four, five or more of these immunogenic epitopes. The polypeptides comprising one or more immunogenic epitopes may be presented for eliciting an antibody response together with a carrier protein, such as an albumin, to

an animal system (such as rabbit or mouse), or, if the polypeptide is of sufficient length (at least about 25 amino acids), the polypeptide may be presented without a carrier. However, immunogenic epitopes comprising as few as 8 to 10 amino acids have been shown to be sufficient to raise antibodies capable of binding to, at the very least, linear epitopes in a denatured polypeptide (e.g., in Western blotting).

Epitope-bearing polypeptides of the present invention may be used to induce antibodies according to methods well known in the art including, but not limited to, in vivo immunization, in vitro immunization, and phage display methods. See, e.g., Sutcliffe et al., supra; Wilson et al., supra, and Bittle et al., J. Gen. Virol., 66:2347-2354 (1985). If in vivo immunization is used, animals may be immunized with free peptide; however, anti-peptide antibody titer may be boosted by coupling the peptide to a macromolecular carrier, such as keyhole limpet hemacyanin (KLH) or tetanus toxoid. For instance, peptides containing cysteine residues may be coupled to a carrier using a linker such as maleimidobenzoyl- N-hydroxysuccinimide ester (MBS), while other peptides may be coupled to carriers using a more general linking agent such as glutaraldehyde. Animals such as rabbits, rats and mice are immunized with either free or carrier- coupled peptides, for instance, by intraperitoneal and/or intradermal injection of emulsions containing about 100 μg of peptide or carrier protein and Freund's adjuvant or any other adjuvant known for stimulating an immune response. Several booster injections may be needed, for instance, at intervals of about two weeks, to provide a useful titer of anti-peptide antibody which can be detected, for example, by ELISA assay using free peptide adsorbed to a solid surface. The titer of anti-peptide antibodies in serum from an immunized animal may be increased by selection of anti-peptide antibodies, for instance, by adsorption to the peptide on a solid support and elution of the selected antibodies according to methods well known in the art.

As one of skill in the art will appreciate, and as discussed above, the polypeptides of the present invention (e.g., those comprising an immunogenic or antigenic epitope) can be fused to heterologous polypeptide sequences. For example, polypeptides of the present invention (including fragments or variants thereof), may be fused with the constant domain of immunoglobulins (IgA, IgE, IgG, IgM), or portions thereof (CH1, CH2, CH3, or any combination thereof and portions thereof,

resulting in chimeric polypeptides. By way of another non-limiting example, polypeptides and/or antibodies of the present invention (including fragments or variants thereof) may be fused with albumin (including but not limited to recombinant human serum albumin or fragments or variants thereof (see, e.g., U.S. Patent No. 5,876,969, issued March 2, 1999, EP Patent 0 413 622, and U.S. Patent No. 5,766,883, issued June 16, 1998, herein incorporated by reference in their entirety)). In a preferred embodiment, polypeptides and/or antibodies of the present invention (including fragments or variants thereof) are fused with the mature form of human serum albumin (i.e., amino acids 1 – 585 of human serum albumin as shown in Figures 1 and 2 of EP Patent 0 322 094) which is herein incorporated by reference in its entirety. In another preferred embodiment, polypeptides and/or antibodies of the present invention (including fragments or variants thereof) are fused with polypeptide fragments comprising, or alternatively consisting of, amino acid residues 1-z of human serum albumin, where z is an integer from 369 to 419, as described in U.S. Patent 5,766,883 herein incorporated by reference in its entirety. Polypeptides and/or antibodies of the present invention (including fragments or variants thereof) may be fused to either the N- or C-terminal end of the heterologous protein (e.g., immunoglobulin Fc polypeptide or human serum albumin polypeptide). Polynucleotides encoding fusion proteins of the invention are also encompassed by the invention.

Such fusion proteins may facilitate purification and may increase half-life in vivo. This has been shown for chimeric proteins consisting of the first two domains of the human CD4-polypeptide and various domains of the constant regions of the heavy or light chains of mammalian immunoglobulins. See, e.g., EP 394,827; Traunecker et al., Nature, 331:84-86 (1988). Enhanced delivery of an antigen across the epithelial barrier to the immune system has been demonstrated for antigens (e.g., insulin) conjugated to an FcRn binding partner such as IgG or Fc fragments (see, e.g., PCT Publications WO 96/22024 and WO 99/04813). IgG Fusion proteins that have a disulfide-linked dimeric structure due to the IgG portion desulfide bonds have also been found to be more efficient in binding and neutralizing other molecules than monomeric polypeptides or fragments thereof alone. See, e.g., Fountoulakis et al., J. Biochem., 270:3958-3964 (1995). Nucleic acids encoding the above epitopes can

also be recombined with a gene of interest as an epitope tag (e.g., the hemagglutinin ("HA") tag or flag tag) to aid in detection and purification of the expressed polypeptide. For example, a system described by Janknecht et al. allows for the ready purification of non-denatured fusion proteins expressed in human cell lines (Janknecht et al., 1991, Proc. Natl. Acad. Sci. USA 88:8972- 897). In this system, the gene of interest is subcloned into a vaccinia recombination plasmid such that the open reading frame of the gene is translationally fused to an amino-terminal tag consisting of six histidine residues. The tag serves as a matrix binding domain for the fusion protein. Extracts from cells infected with the recombinant vaccinia virus are loaded onto Ni2+ nitriloacetic acid-agarose column and histidine-tagged proteins can be selectively eluted with imidazole-containing buffers.

Additional fusion proteins of the invention may be generated through the techniques of gene-shuffling, motif-shuffling, exon-shuffling, and/or codon-shuffling (collectively referred to as "DNA shuffling"). DNA shuffling may be employed to modulate the activities of polypeptides of the invention, such methods can be used to generate polypeptides with altered activity, as well as agonists and antagonists of the polypeptides. See, generally, U.S. Patent Nos. 5,605,793; 5,811,238; 5,830,721; 5,834,252; and 5,837,458, and Patten et al., Curr. Opinion Biotechnol. 8:724-33 (1997); Harayama, Trends Biotechnol. 16(2):76-82 (1998); Hansson, et al., J. Mol. Biol. 287:265-76 (1999); and Lorenzo and Blasco, Biotechniques 24(2):308- 13 (1998) (each of these patents and publications are hereby incorporated by reference in its entirety). In one embodiment, alteration of polynucleotides corresponding to SEQ ID NO:X and the polypeptides encoded by these polynucleotides may be achieved by DNA shuffling. DNA shuffling involves the assembly of two or more DNA segments by homologous or site-specific recombination to generate variation in the polynucleotide sequence. In another embodiment, polynucleotides of the invention, or the encoded polypeptides, may be altered by being subjected to random mutagenesis by error-prone PCR, random nucleotide insertion or other methods prior to recombination. In another embodiment, one or more components, motifs, sections, parts, domains, fragments, etc., of a polynucleotide encoding a polypeptide of the invention may be recombined with one or more components, motifs, sections, parts, domains, fragments, etc. of one or more heterologous molecules.

Antibodies

Further polypeptides of the invention relate to antibodies and T-cell antigen receptors (TCR) which immunospecifically bind a polypeptide, polypeptide fragment, or variant of SEQ ID NO:Y, and/or an epitope, of the present invention (as determined by immunoassays well known in the art for assaying specific antibody-antigen binding). Antibodies of the invention include, but are not limited to, polyclonal, monoclonal, multispecific, human, humanized or chimeric antibodies, single chain antibodies, Fab fragments, F(ab') fragments, fragments produced by a Fab expression library, anti-idiotypic (anti-Id) antibodies (including, e.g., anti-Id antibodies to antibodies of the invention), and epitope-binding fragments of any of the above. The term "antibody," as used herein, refers to immunoglobulin molecules and immunologically active portions of immunoglobulin molecules, i.e., molecules that contain an antigen binding site that immunospecifically binds an antigen. The immunoglobulin molecules of the invention can be of any type (e.g., IgG, IgE, IgM, IgD, IgA and IgY), class (e.g., IgG1, IgG2, IgG3, IgG4, IgA1 and IgA2) or subclass of immunoglobulin molecule. In preferred embodiments, the immunoglobulin molecules of the invention are IgG1. In other preferred embodiments, the immunoglobulin molecules of the invention are IgG4.

Most preferably the antibodies are human antigen-binding antibody fragments of the present invention and include, but are not limited to, Fab, Fab' and F(ab')2, Fd, single-chain Fvs (scFv), single-chain antibodies, disulfide-linked Fvs (sdFv) and fragments comprising either a VL or VH domain. Antigen-binding antibody fragments, including single-chain antibodies, may comprise the variable region(s) alone or in combination with the entirety or a portion of the following: hinge region, CH1, CH2, and CH3 domains. Also included in the invention are antigen-binding fragments also comprising any combination of variable region(s) with a hinge region, CH1, CH2, and CH3 domains. The antibodies of the invention may be from any animal origin including birds and mammals. Preferably, the antibodies are human, murine (e.g., mouse and rat), donkey, ship rabbit, goat, guinea pig, camel, horse, or chicken. As used herein, "human" antibodies include antibodies having the amino acid sequence of a human immunoglobulin and include antibodies isolated from

human immunoglobulin libraries or from animals transgenic for one or more human immunoglobulin and that do not express endogenous immunoglobulins, as described infra and, for example in, U.S. Patent No. 5,939,598 by Kucherlapati et al.

The antibodies of the present invention may be monospecific, bispecific, trispecific or of greater multispecificity. Multispecific antibodies may be specific for different epitopes of a polypeptide of the present invention or may be specific for both a polypeptide of the present invention as well as for a heterologous epitope, such as a heterologous polypeptide or solid support material. See, e.g., PCT publications WO 93/17715; WO 92/08802; WO 91/00360; WO 92/05793; Tutt, et al., J. Immunol. 147:60-69 (1991); U.S. Patent Nos. 4,474,893; 4,714,681; 4,925,648; 5,573,920; 5,601,819; Kostelny et al., J. Immunol. 148:1547-1553 (1992).

Antibodies of the present invention may be described or specified in terms of the epitope(s) or portion(s) of a polypeptide of the present invention which they recognize or specifically bind. The epitope(s) or polypeptide portion(s) may be specified as described herein, e.g., by N-terminal and C-terminal positions, by size in contiguous amino acid residues, or listed in the Tables and Figures. Antibodies which specifically bind any epitope or polypeptide of the present invention may also be excluded. Therefore, the present invention includes antibodies that specifically bind polypeptides of the present invention, and allows for the exclusion of the same.

Antibodies of the present invention may also be described or specified in terms of their cross-reactivity. Antibodies that do not bind any other analog, ortholog, or homolog of a polypeptide of the present invention are included. Antibodies that bind polypeptides with at least 95%, at least 90%, at least 85%, at least 80%, at least 75%, at least 70%, at least 65%, at least 60%, at least 55%, and at least 50% identity (as calculated using methods known in the art and described herein) to a polypeptide of the present invention are also included in the present invention. In specific embodiments, antibodies of the present invention cross-react with murine, rat and/or rabbit homologs of human proteins and the corresponding epitopes thereof. Antibodies that do not bind polypeptides with less than 95%, less than 90%, less than 85%, less than 80%, less than 75%, less than 70%, less than 65%, less than 60%, less than 55%, and less than 50% identity (as calculated using methods known in the art and described herein) to a polypeptide of the present

invention are also included in the present invention. In a specific embodiment, the above-described cross-reactivity is with respect to any single specific antigenic or immunogenic polypeptide, or combination(s) of 2, 3, 4, 5, or more of the specific antigenic and/or immunogenic polypeptides disclosed herein. Further included in the present invention are antibodies which bind polypeptides encoded by polynucleotides which hybridize to a polynucleotide of the present invention under stringent hybridization conditions (as described herein). Antibodies of the present invention may also be described or specified in terms of their binding affinity to a polypeptide of the invention. Preferred binding affinities include those with a dissociation constant or Kd less than 5 X 10^{-2} M, 10^{-2} M, 5 X 10^{-3} M, 10^{-3} M, 5 X 10^{-4} M, 10^{-4} M, 5 X 10^{-5} M, 10^{-5} M, 5 X 10^{-6} M, 10^{-6}M, 5 X 10^{-7} M, 10^{7} M, 5 X 10^{-8} M, 10^{-8} M, 5 X 10^{-9} M, 10^{-9} M, 5 X 10^{-10} M, 10^{-10} M, 5 X 10^{-11} M, 10^{-11} M, 5 X 10^{-12} M, $^{10-12}$ M, 5 X 10^{-13} M, 10^{-13} M, 5 X 10^{-14} M, 10^{-14} M, 5 X 10^{-15} M, or 10^{-15} M.

The invention also provides antibodies that competitively inhibit binding of an antibody to an epitope of the invention as determined by any method known in the art for determining competitive binding, for example, the immunoassays described herein. In preferred embodiments, the antibody competitively inhibits binding to the epitope by at least 95%, at least 90%, at least 85 %, at least 80%, at least 75%, at least 70%, at least 60%, or at least 50%.

Antibodies of the present invention may act as agonists or antagonists of the polypeptides of the present invention. For example, the present invention includes antibodies which disrupt the receptor/ligand interactions with the polypeptides of the invention either partially or fully. Preferrably, antibodies of the present invention bind an antigenic epitope disclosed herein, or a portion thereof. The invention features both receptor-specific antibodies and ligand-specific antibodies. The invention also features receptor-specific antibodies which do not prevent ligand binding but prevent receptor activation. Receptor activation (i.e., signaling) may be determined by techniques described herein or otherwise known in the art. For example, receptor activation can be determined by detecting the phosphorylation (e.g., tyrosine or serine/threonine) of the receptor or its substrate by immunoprecipitation followed by western blot analysis (for example, as described supra). In specific embodiments, antibodies are provided that inhibit ligand activity

or receptor activity by at least 95%, at least 90%, at least 85%, at least 80%, at least 75%, at least 70%, at least 60%, or at least 50% of the activity in absence of the antibody.

The invention also features receptor-specific antibodies which both prevent ligand binding and receptor activation as well as antibodies that recognize the receptor-ligand complex, and, preferably, do not specifically recognize the unbound receptor or the unbound ligand. Likewise, included in the invention are neutralizing antibodies which bind the ligand and prevent binding of the ligand to the receptor, as well as antibodies which bind the ligand, thereby preventing receptor activation, but do not prevent the ligand from binding the receptor. Further included in the invention are antibodies which activate the receptor. These antibodies may act as receptor agonists, i.e., potentiate or activate either all or a subset of the biological activities of the ligand-mediated receptor activation, for example, by inducing dimerization of the receptor. The antibodies may be specified as agonists, antagonists or inverse agonists for biological activities comprising the specific biological activities of the peptides of the invention disclosed herein. The above antibody agonists can be made using methods known in the art. See, e.g., PCT publication WO 96/40281; U.S. Patent No. 5,811,097; Deng et al., Blood 92(6):1981-1988 (1998); Chen et al., Cancer Res. 58(16):3668-3678 (1998); Harrop et al., J. Immunol. 161(4):1786-1794 (1998); Zhu et al., Cancer Res. 58(15):3209-3214 (1998); Yoon et al., J. Immunol. 160(7):3170-3179 (1998); Prat et al., J. Cell. Sci. 111(Pt2):237-247 (1998); Pitard et al., J. Immunol. Methods 205(2):177-190 (1997); Liautard et al., Cytokine 9(4):233-241 (1997); Carlson et al., J. Biol. Chem. 272(17):11295-11301 (1997); Taryman et al., Neuron 14(4):755-762 (1995); Muller et al., Structure 6(9):1153-1167 (1998); Bartunek et al., Cytokine 8(1):14-20 (1996) (which are all incorporated by reference herein in their entireties).

Antibodies of the present invention may be used, for example, but not limited to, to purify, detect, and target the polypeptides of the present invention, including both in vitro and in vivo diagnostic and therapeutic methods. For example, the antibodies have use in immunoassays for qualitatively and quantitatively measuring levels of the polypeptides of the present invention in biological samples. See, e.g.,

Harlow et al., Antibodies: A Laboratory Manual, (Cold Spring Harbor Laboratory Press, 2nd ed. 1988) (incorporated by reference herein in its entirety).

As discussed in more detail below, the antibodies of the present invention may be used either alone or in combination with other compositions. The antibodies may further be recombinantly fused to a heterologous polypeptide at the N- or C-terminus or chemically conjugated (including covalently and non-covalently conjugations) to polypeptides or other compositions. For example, antibodies of the present invention may be recombinantly fused or conjugated to molecules useful as labels in detection assays and effector molecules such as heterologous polypeptides, drugs, radionuclides, or toxins. See, e.g., PCT publications WO 92/08495; WO 91/14438; WO 89/12624; U.S. Patent No. 5,314,995; and EP 396,387.

The antibodies of the invention include derivatives that are modified, i.e, by the covalent attachment of any type of molecule to the antibody such that covalent attachment does not prevent the antibody from generating an anti-idiotypic response. For example, but not by way of limitation, the antibody derivatives include antibodies that have been modified, e.g., by glycosylation, acetylation, pegylation, phosphylation, amidation, derivatization by known protecting/blocking groups, proteolytic cleavage, linkage to a cellular ligand or other protein, etc. Any of numerous chemical modifications may be carried out by known techniques, including, but not limited to specific chemical cleavage, acetylation, formylation, metabolic synthesis of tunicamycin, etc. Additionally, the derivative may contain one or more non-classical amino acids.

The antibodies of the present invention may be generated by any suitable method known in the art. Polyclonal antibodies to an antigen-of- interest can be produced by various procedures well known in the art. For example, a polypeptide of the invention can be administered to various host animals including, but not limited to, rabbits, mice, rats, etc. to induce the production of sera containing polyclonal antibodies specific for the antigen. Various adjuvants may be used to increase the immunological response, depending on the host species, and include but are not limited to, Freund's (complete and incomplete), mineral gels such as aluminum hydroxide, surface active substances such as lysolecithin, pluronic polyols, polyanions, peptides, oil emulsions, keyhole limpet hemocyanins, dinitrophenol, and

potentially useful human adjuvants such as BCG (bacille Calmette-Guerin) and corynebacterium parvum. Such adjuvants are also well known in the art.

Monoclonal antibodies can be prepared using a wide variety of techniques known in the art including the use of hybridoma, recombinant, and phage display technologies, or a combination thereof. For example, monoclonal antibodies can be produced using hybridoma techniques including those known in the art and taught, for example, in Harlow et al., Antibodies: A Laboratory Manual, (Cold Spring Harbor Laboratory Press, 2nd ed. 1988); Hammerling, et al., in: Monoclonal Antibodies and T-Cell Hybridomas 563-681 (Elsevier, N.Y., 1981) (said references incorporated by reference in their entireties). The term "monoclonal antibody" as used herein is not limited to antibodies produced through hybridoma technology. The term "monoclonal antibody" refers to an antibody that is derived from a single clone, including any eukaryotic, prokaryotic, or phage clone, and not the method by which it is produced.

Methods for producing and screening for specific antibodies using hybridoma technology are routine and well known in the art and are discussed in detail in the Examples (e.g., Example 16). In a non-limiting example, mice can be immunized with a polypeptide of the invention or a cell expressing such peptide. Once an immune response is detected, e.g., antibodies specific for the antigen are detected in the mouse serum, the mouse spleen is harvested and splenocytes isolated. The splenocytes are then fused by well known techniques to any suitable myeloma cells, for example cells from cell line SP20 available from the ATCC. Hybridomas are selected and cloned by limited dilution. The hybridoma clones are then assayed by methods known in the art for cells that secrete antibodies capable of binding a polypeptide of the invention. Ascites fluid, which generally contains high levels of antibodies, can be generated by immunizing mice with positive hybridoma clones.

Accordingly, the present invention provides methods of generating monoclonal antibodies as well as antibodies produced by the method comprising culturing a hybridoma cell secreting an antibody of the invention wherein, preferably, the hybridoma is generated by fusing splenocytes isolated from a mouse immunized with an antigen of the invention with myeloma cells and then screening the

hybridomas resulting from the fusion for hybridoma clones that secrete an antibody able to bind a polypeptide of the invention.

Antibody fragments which recognize specific epitopes may be generated by known techniques. For example, Fab and F(ab')2 fragments of the invention may be produced by proteolytic cleavage of immunoglobulin molecules, using enzymes such as papain (to produce Fab fragments) or pepsin (to produce F(ab')2 fragments). F(ab')2 fragments contain the variable region, the light chain constant region and the CH1 domain of the heavy chain.

For example, the antibodies of the present invention can also be generated using various phage display methods known in the art. In phage display methods, functional antibody domains are displayed on the surface of phage particles which carry the polynucleotide sequences encoding them. In a particular embodiment, such phage can be utilized to display antigen binding domains expressed from a repertoire or combinatorial antibody library (e.g., human or murine). Phage expressing an antigen binding domain that binds the antigen of interest can be selected or identified with antigen, e.g., using labeled antigen or antigen bound or captured to a solid surface or bead. Phage used in these methods are typically filamentous phage including fd and M13 binding domains expressed from phage with Fab, Fv or disulfide stabilized Fv antibody domains recombinantly fused to either the phage gene III or gene VIII protein. Examples of phage display methods that can be used to make the antibodies of the present invention include those disclosed in Brinkman et al., J. Immunol. Methods 182:41-50 (1995); Ames et al., J. Immunol. Methods 184:177-186 (1995); Kettleborough et al., Eur. J. Immunol. 24:952-958 (1994); Persic et al., Gene 187 9-18 (1997); Burton et al., Advances in Immunology 57:191-280 (1994); PCT application No. PCT/GB91/01134; PCT publications WO 90/02809; WO 91/10737; WO 92/01047; WO 92/18619; WO 93/11236; WO 95/15982; WO 95/20401; and U.S. Patent Nos. 5,698,426; 5,223,409; 5,403,484; 5,580,717; 5,427,908; 5,750,753; 5,821,047; 5,571,698; 5,427,908; 5,516,637; 5,780,225; 5,658,727; 5,733,743 and 5,969,108; each of which is incorporated herein by reference in its entirety.

As described in the above references, after phage selection, the antibody coding regions from the phage can be isolated and used to generate whole antibodies,

including human antibodies, or any other desired antigen binding fragment, and expressed in any desired host, including mammalian cells, insect cells, plant cells, yeast, and bacteria, e.g., as described in detail below. For example, techniques to recombinantly produce Fab, Fab' and F(ab')2 fragments can also be employed using methods known in the art such as those disclosed in PCT publication WO 92/22324; Mullinax et al., BioTechniques 12(6):864-869 (1992); and Sawai et al., AJRI 34:26-34 (1995); and Better et al., Science 240:1041-1043 (1988) (said references incorporated by reference in their entireties).

Examples of techniques which can be used to produce single-chain Fvs and antibodies include those described in U.S. Patents 4,946,778 and 5,258,498; Huston et al., Methods in Enzymology 203:46-88 (1991); Shu et al., PNAS 90:7995-7999 (1993); and Skerra et al., Science 240:1038-1040 (1988). For some uses, including in vivo use of antibodies in humans and in vitro detection assays, it may be preferable to use chimeric, humanized, or human antibodies. A chimeric antibody is a molecule in which different portions of the antibody are derived from different animal species, such as antibodies having a variable region derived from a murine monoclonal antibody and a human immunoglobulin constant region. Methods for producing chimeric antibodies are known in the art. See e.g., Morrison, Science 229:1202 (1985); Oi et al., BioTechniques 4:214 (1986); Gillies et al., (1989) J. Immunol. Methods 125:191-202; U.S. Patent Nos. 5,807,715; 4,816,567; and 4,816397, which are incorporated herein by reference in their entirety. Humanized antibodies are antibody molecules from non-human species antibody that binds the desired antigen having one or more complementarity determining regions (CDRs) from the non-human species and a framework regions from a human immunoglobulin molecule. Often, framework residues in the human framework regions will be substituted with the corresponding residue from the CDR donor antibody to alter, preferably improve, antigen binding. These framework substitutions are identified by methods well known in the art, e.g., by modeling of the interactions of the CDR and framework residues to identify framework residues important for antigen binding and sequence comparison to identify unusual framework residues at particular positions. (See, e.g., Queen et al., U.S. Patent No. 5,585,089; Riechmann et al., Nature 332:323 (1988), which are incorporated herein by reference in their entireties.) Antibodies can be

humanized using a variety of techniques known in the art including, for example, CDR-grafting (EP 239,400; PCT publication WO 91/09967; U.S. Patent Nos. 5,225,539; 5,530,101; and 5,585,089), veneering or resurfacing (EP 592,106; EP 519,596; Padlan, Molecular Immunology 28(4/5):489-498 (1991); Studnicka et al., Protein Engineering 7(6):805-814 (1994); Roguska. et al., PNAS 91:969-973 (1994)), and chain shuffling (U.S. Patent No. 5,565,332).

Completely human antibodies are particularly desirable for therapeutic treatment of human patients. Human antibodies can be made by a variety of methods known in the art including phage display methods described above using antibody libraries derived from human immunoglobulin sequences. See also, U.S. Patent Nos. 4,444,887 and 4,716,111; and PCT publications WO 98/46645, WO 98/50433, WO 98/24893, WO 98/16654, WO 96/34096, WO 96/33735, and WO 91/10741; each of which is incorporated herein by reference in its entirety.

Human antibodies can also be produced using transgenic mice which are incapable of expressing functional endogenous immunoglobulins, but which can express human immunoglobulin genes. For example, the human heavy and light chain immunoglobulin gene complexes may be introduced randomly or by homologous recombination into mouse embryonic stem cells. Alternatively, the human variable region, constant region, and diversity region may be introduced into mouse embryonic stem cells in addition to the human heavy and light chain genes. The mouse heavy and light chain immunoglobulin genes may be rendered non-functional separately or simultaneously with the introduction of human immunoglobulin loci by homologous recombination. In particular, homozygous deletion of the JH region prevents endogenous antibody production. The modified embryonic stem cells are expanded and microinjected into blastocysts to produce chimeric mice. The chimeric mice are then bred to produce homozygous offspring which express human antibodies. The transgenic mice are immunized in the normal fashion with a selected antigen, e.g., all or a portion of a polypeptide of the invention. Monoclonal antibodies directed against the antigen can be obtained from the immunized, transgenic mice using conventional hybridoma technology. The human immunoglobulin transgenes harbored by the transgenic mice rearrange during B cell differentiation, and subsequently undergo class switching and somatic mutation.

Thus, using such a technique, it is possible to produce therapeutically useful IgG, IgA, IgM and IgE antibodies. For an overview of this technology for producing human antibodies, see Lonberg and Huszar, Int. Rev. Immunol. 13:65-93 (1995). For a detailed discussion of this technology for producing human antibodies and human monoclonal antibodies and protocols for producing such antibodies, see, e.g., PCT publications WO 98/24893; WO 92/01047; WO 96/34096; WO 96/33735; European Patent No. 0 598 877; U.S. Patent Nos. 5,413,923; 5,625,126; 5,633,425; 5,569,825; 5,661,016; 5,545,806; 5,814,318; 5,885;793; 5,916,771; and 5,939,598, which are incorporated by reference herein in their entirety. In addition, companies such as Abgenix, Inc. (Freemont, CA) and Genpharm (San Jose, CA) can be engaged to provide human antibodies directed against a selected antigen using technology similar to that described above.

Completely human antibodies which recognize a selected epitope can be generated using a technique referred to as "guided selection." In this approach a selected non-human monoclonal antibody, e.g., a mouse antibody, is used to guide the selection of a completely human antibody recognizing the same epitope. (Jespers et al., Bio/technology 12:899-903 (1988)).

Further, antibodies to the polypeptides of the invention can, in turn, be utilized to generate anti-idiotype antibodies that "mimic" polypeptides of the invention using techniques well known to those skilled in the art. (See, e.g., Greenspan & Bona, FASEB J. 7(5):437-444; (1989) and Nissinoff, J. Immunol. 147(8):2429-2438 (1991)). For example, antibodies which bind to and competitively inhibit polypeptide multimerization and/or binding of a polypeptide of the invention to a ligand can be used to generate anti-idiotypes that "mimic" the polypeptide multimerization and/or binding domain and, as a consequence, bind to and neutralize polypeptide and/or its ligand. Such neutralizing anti-idiotypes or Fab fragments of such anti-idiotypes can be used in therapeutic regimens to neutralize polypeptide ligand. For example, such anti-idiotypic antibodies can be used to bind a polypeptide of the invention and/or to bind its ligands/receptors, and thereby block its biological activity.

Polynucleotides Encoding Antibodies

The invention further provides polynucleotides comprising a nucleotide sequence encoding an antibody of the invention and fragments thereof. The invention also encompasses polynucleotides that hybridize under stringent or lower stringency hybridization conditions, e.g., as defined supra, to polynucleotides that encode an antibody, preferably, that specifically binds to a polypeptide of the invention, preferably, an antibody that binds to a polypeptide having the amino acid sequence of SEQ ID NO:Y.

The polynucleotides may be obtained, and the nucleotide sequence of the polynucleotides determined, by any method known in the art. For example, if the nucleotide sequence of the antibody is known, a polynucleotide encoding the antibody may be assembled from chemically synthesized oligonucleotides (e.g., as described in Kutmeier et al., BioTechniques 17:242 (1994)), which, briefly, involves the synthesis of overlapping oligonucleotides containing portions of the sequence encoding the antibody, annealing and ligating of those oligonucleotides, and then amplification of the ligated oligonucleotides by PCR.

Alternatively, a polynucleotide encoding an antibody may be generated from nucleic acid from a suitable source. If a clone containing a nucleic acid encoding a particular antibody is not available, but the sequence of the antibody molecule is known, a nucleic acid encoding the immunoglobulin may be chemically synthesized or obtained from a suitable source (e.g., an antibody cDNA library, or a cDNA library generated from, or nucleic acid, preferably poly A+ RNA, isolated from, any tissue or cells expressing the antibody, such as hybridoma cells selected to express an antibody of the invention) by PCR amplification using synthetic primers hybridizable to the 3' and 5' ends of the sequence or by cloning using an oligonucleotide probe specific for the particular gene sequence to identify, e.g., a cDNA clone from a cDNA library that encodes the antibody. Amplified nucleic acids generated by PCR may then be cloned into replicable cloning vectors using any method well known in the art.

Once the nucleotide sequence and corresponding amino acid sequence of the antibody is determined, the nucleotide sequence of the antibody may be manipulated using methods well known in the art for the manipulation of nucleotide sequences, e.g., recombinant DNA techniques, site directed mutagenesis, PCR, etc. (see, for

example, the techniques described in Sambrook et al., 1990, Molecular Cloning, A Laboratory Manual, 2d Ed., Cold Spring Harbor Laboratory, Cold Spring Harbor, NY and Ausubel et al., eds., 1998, Current Protocols in Molecular Biology, John Wiley & Sons, NY, which are both incorporated by reference herein in their entireties), to generate antibodies having a different amino acid sequence, for example to create amino acid substitutions, deletions, and/or insertions.

In a specific embodiment, the amino acid sequence of the heavy and/or light chain variable domains may be inspected to identify the sequences of the complementarity determining regions (CDRs) by methods that are well know in the art, e.g., by comparison to known amino acid sequences of other heavy and light chain variable regions to determine the regions of sequence hypervariability. Using routine recombinant DNA techniques, one or more of the CDRs may be inserted within framework regions, e.g., into human framework regions to humanize a non-human antibody, as described supra. The framework regions may be naturally occurring or consensus framework regions, and preferably human framework regions (see, e.g., Chothia et al., J. Mol. Biol. 278: 457-479 (1998) for a listing of human framework regions). Preferably, the polynucleotide generated by the combination of the framework regions and CDRs encodes an antibody that specifically binds a polypeptide of the invention. Preferably, as discussed supra, one or more amino acid substitutions may be made within the framework regions, and, preferably, the amino acid substitutions improve binding of the antibody to its antigen. Additionally, such methods may be used to make amino acid substitutions or deletions of one or more variable region cysteine residues participating in an intrachain disulfide bond to generate antibody molecules lacking one or more intrachain disulfide bonds. Other alterations to the polynucleotide are encompassed by the present invention and within the skill of the art.

In addition, techniques developed for the production of "chimeric antibodies" (Morrison et al., Proc. Natl. Acad. Sci. 81:851-855 (1984); Neuberger et al., Nature 312:604-608 (1984); Takeda et al., Nature 314:452-454 (1985)) by splicing genes from a mouse antibody molecule of appropriate antigen specificity together with genes from a human antibody molecule of appropriate biological activity can be used. As described supra, a chimeric antibody is a molecule in which different portions are

derived from different animal species, such as those having a variable region derived from a murine mAb and a human immunoglobulin constant region, e.g., humanized antibodies.

Alternatively, techniques described for the production of single chain antibodies (U.S. Patent No. 4,946,778; Bird, Science 242:423- 42 (1988); Huston et al., Proc. Natl. Acad. Sci. USA 85:5879-5883 (1988); and Ward et al., Nature 334:544-54 (1989)) can be adapted to produce single chain antibodies. Single chain antibodies are formed by linking the heavy and light chain fragments of the Fv region via an amino acid bridge, resulting in a single chain polypeptide. Techniques for the assembly of functional Fv fragments in E. coli may also be used (Skerra et al., Science 242:1038- 1041 (1988)).

Methods of Producing Antibodies

The antibodies of the invention can be produced by any method known in the art for the synthesis of antibodies, in particular, by chemical synthesis or preferably, by recombinant expression techniques.

Recombinant expression of an antibody of the invention, or fragment, derivative or analog thereof, (e.g., a heavy or light chain of an antibody of the invention or a single chain antibody of the invention), requires construction of an expression vector containing a polynucleotide that encodes the antibody. Once a polynucleotide encoding an antibody molecule or a heavy or light chain of an antibody, or portion thereof (preferably containing the heavy or light chain variable domain), of the invention has been obtained, the vector for the production of the antibody molecule may be produced by recombinant DNA technology using techniques well known in the art. Thus, methods for preparing a protein by expressing a polynucleotide containing an antibody encoding nucleotide sequence are described herein. Methods which are well known to those skilled in the art can be used to construct expression vectors containing antibody coding sequences and appropriate transcriptional and translational control signals. These methods include, for example, in vitro recombinant DNA techniques, synthetic techniques, and in vivo genetic recombination. The invention, thus, provides replicable vectors comprising a nucleotide sequence encoding an antibody molecule of the invention, or a heavy or

light chain thereof, or a heavy or light chain variable domain, operably linked to a promoter. Such vectors may include the nucleotide sequence encoding the constant region of the antibody molecule (see, e.g., PCT Publication WO 86/05807; PCT Publication WO 89/01036; and U.S. Patent No. 5,122,464) and the variable domain of the antibody may be cloned into such a vector for expression of the entire heavy or light chain.

The expression vector is transferred to a host cell by conventional techniques and the transfected cells are then cultured by conventional techniques to produce an antibody of the invention. Thus, the invention includes host cells containing a polynucleotide encoding an antibody of the invention, or a heavy or light chain thereof, or a single chain antibody of the invention, operably linked to a heterologous promoter. In preferred embodiments for the expression of double-chained antibodies, vectors encoding both the heavy and light chains may be co-expressed in the host cell for expression of the entire immunoglobulin molecule, as detailed below.

A variety of host-expression vector systems may be utilized to express the antibody molecules of the invention. Such host-expression systems represent vehicles by which the coding sequences of interest may be produced and subsequently purified, but also represent cells which may, when transformed or transfected with the appropriate nucleotide coding sequences, express an antibody molecule of the invention in situ. These include but are not limited to microorganisms such as bacteria (e.g., E. coli, B. subtilis) transformed with recombinant bacteriophage DNA, plasmid DNA or cosmid DNA expression vectors containing antibody coding sequences; yeast (e.g., Saccharomyces, Pichia) transformed with recombinant yeast expression vectors containing antibody coding sequences; insect cell systems infected with recombinant virus expression vectors (e.g., baculovirus) containing antibody coding sequences; plant cell systems infected with recombinant virus expression vectors (e.g., cauliflower mosaic virus, CaMV; tobacco mosaic virus, TMV) or transformed with recombinant plasmid expression vectors (e.g., Ti plasmid) containing antibody coding sequences; or mammalian cell systems (e.g., COS, CHO, BHK, 293, 3T3 cells) harboring recombinant expression constructs containing promoters derived from the genome of mammalian cells (e.g., metallothionein promoter) or from mammalian viruses (e.g., the adenovirus late promoter; the

vaccinia virus 7.5K promoter). Preferably, bacterial cells such as Escherichia coli, and more preferably, eukaryotic cells, especially for the expression of whole recombinant antibody molecule, are used for the expression of a recombinant antibody molecule. For example, mammalian cells such as Chinese hamster ovary cells (CHO), in conjunction with a vector such as the major intermediate early gene promoter element from human cytomegalovirus is an effective expression system for antibodies (Foecking et al., Gene 45:101 (1986); Cockett et al., Bio/Technology 8:2 (1990)).

In bacterial systems, a number of expression vectors may be advantageously selected depending upon the use intended for the antibody molecule being expressed. For example, when a large quantity of such a protein is to be produced, for the generation of pharmaceutical compositions of an antibody molecule, vectors which direct the expression of high levels of fusion protein products that are readily purified may be desirable. Such vectors include, but are not limited, to the E. coli expression vector pUR278 (Ruther et al., EMBO J. 2:1791 (1983)), in which the antibody coding sequence may be ligated individually into the vector in frame with the lac Z coding region so that a fusion protein is produced; pIN vectors (Inouye & Inouye, Nucleic Acids Res. 13:3101-3109 (1985); Van Heeke & Schuster, J. Biol. Chem. 24:5503-5509 (1989)); and the like. pGEX vectors may also be used to express foreign polypeptides as fusion proteins with glutathione S-transferase (GST). In general, such fusion proteins are soluble and can easily be purified from lysed cells by adsorption and binding to matrix glutathione-agarose beads followed by elution in the presence of free glutathione. The pGEX vectors are designed to include thrombin or factor Xa protease cleavage sites so that the cloned target gene product can be released from the GST moiety.

In an insect system, Autographa californica nuclear polyhedrosis virus (AcNPV) is used as a vector to express foreign genes. The virus grows in *Spodoptera frugiperda* cells. The antibody coding sequence may be cloned individually into non-essential regions (for example the polyhedrin gene) of the virus and placed under control of an AcNPV promoter (for example the polyhedrin promoter).

In mammalian host cells, a number of viral-based expression systems may be utilized. In cases where an adenovirus is used as an expression vector, the antibody coding sequence of interest may be ligated to an adenovirus transcription/translation control complex, e.g., the late promoter and tripartite leader sequence. This chimeric gene may then be inserted in the adenovirus genome by in vitro or in vivo recombination. Insertion in a non- essential region of the viral genome (e.g., region El or E3) will result in a recombinant virus that is viable and capable of expressing the antibody molecule in infected hosts. (e.g., see Logan & Shenk, Proc. Natl. Acad. Sci. USA 81:355-359 (1984)). Specific initiation signals may also be required for efficient translation of inserted antibody coding sequences. These signals include the ATG initiation codon and adjacent sequences. Furthermore, the initiation codon must be in phase with the reading frame of the desired coding sequence to ensure translation of the entire insert. These exogenous translational control signals and initiation codons can be of a variety of origins, both natural and synthetic. The efficiency of expression may be enhanced by the inclusion of appropriate transcription enhancer elements, transcription terminators, etc. (see Bittner et al., Methods in Enzymol. 153:51-544 (1987)).

In addition, a host cell strain may be chosen which modulates the expression of the inserted sequences, or modifies and processes the gene product in the specific fashion desired. Such modifications (e.g., glycosylation) and processing (e.g., cleavage) of protein products may be important for the function of the protein. Different host cells have characteristic and specific mechanisms for the post-translational processing and modification of proteins and gene products. Appropriate cell lines or host systems can be chosen to ensure the correct modification and processing of the foreign protein expressed. To this end, eukaryotic host cells which possess the cellular machinery for proper processing of the primary transcript, glycosylation, and phosphorylation of the gene product may be used. Such mammalian host cells include but are not limited to CHO, VERY, BHK, Hela, COS, MDCK, 293, 3T3, WI38, and in particular, breast cancer cell lines such as, for example, BT483, Hs578T, HTB2, BT20 and T47D, and normal mammary gland cell line such as, for example, CRL7030 and Hs578Bst.

For long-term, high-yield production of recombinant proteins, stable expression is preferred. For example, cell lines which stably express the antibody molecule may be engineered. Rather than using expression vectors which contain viral origins of replication, host cells can be transformed with DNA controlled by appropriate expression control elements (e.g., promoter, enhancer, sequences, transcription terminators, polyadenylation sites, etc.), and a selectable marker. Following the introduction of the foreign DNA, engineered cells may be allowed to grow for 1-2 days in an enriched media, and then are switched to a selective media. The selectable marker in the recombinant plasmid confers resistance to the selection and allows cells to stably integrate the plasmid into their chromosomes and grow to form foci which in turn can be cloned and expanded into cell lines. This method may advantageously be used to engineer cell lines which express the antibody molecule. Such engineered cell lines may be particularly useful in screening and evaluation of compounds that interact directly or indirectly with the antibody molecule.

A number of selection systems may be used, including but not limited to the herpes simplex virus thymidine kinase (Wigler et al., Cell 11:223 (1977)), hypoxanthine-guanine phosphoribosyltransferase (Szybalska & Szybalski, Proc. Natl. Acad. Sci. USA 48:202 (1992)), and adenine phosphoribosyltransferase (Lowy et al., Cell 22:817 (1980)) genes can be employed in tk-, hgprt- or aprt- cells, respectively. Also, antimetabolite resistance can be used as the basis of selection for the following genes: dhfr, which confers resistance to methotrexate (Wigler et al., Natl. Acad. Sci. USA 77:357 (1980); O'Hare et al., Proc. Natl. Acad. Sci. USA 78:1527 (1981)); gpt, which confers resistance to mycophenolic acid (Mulligan & Berg, Proc. Natl. Acad. Sci. USA 78:2072 (1981)); neo, which confers resistance to the aminoglycoside G-418 Clinical Pharmacy 12:488-505; Wu and Wu, Biotherapy 3:87-95 (1991); Tolstoshev, Ann. Rev. Pharmacol. Toxicol. 32:573-596 (1993); Mulligan, Science 260:926-932 (1993); and Morgan and Anderson, Ann. Rev. Biochem. 62:191-217 (1993); May, 1993, TIB TECH 11(5):155-215); and hygro, which confers resistance to hygromycin (Santerre et al., Gene 30:147 (1984)). Methods commonly known in the art of recombinant DNA technology may be routinely applied to select the desired recombinant clone, and such methods are described, for example, in Ausubel et al. (eds.), Current Protocols in Molecular Biology, John Wiley & Sons, NY (1993);

Kriegler, Gene Transfer and Expression, A Laboratory Manual, Stockton Press, NY (1990); and in Chapters 12 and 13, Dracopoli et al. (eds), Current Protocols in Human Genetics, John Wiley & Sons, NY (1994); Colberre-Garapin et al., J. Mol. Biol. 150:1 (1981), which are incorporated by reference herein in their entireties.

The expression levels of an antibody molecule can be increased by vector amplification (for a review, see Bebbington and Hentschel, The use of vectors based on gene amplification for the expression of cloned genes in mammalian cells in DNA cloning, Vol.3. (Academic Press, New York, 1987)). When a marker in the vector system expressing antibody is amplifiable, increase in the level of inhibitor present in culture of host cell will increase the number of copies of the marker gene. Since the amplified region is associated with the antibody gene, production of the antibody will also increase (Crouse et al., Mol. Cell. Biol. 3:257 (1983)).

The host cell may be co-transfected with two expression vectors of the invention, the first vector encoding a heavy chain derived polypeptide and the second vector encoding a light chain derived polypeptide. The two vectors may contain identical selectable markers which enable equal expression of heavy and light chain polypeptides. Alternatively, a single vector may be used which encodes, and is capable of expressing, both heavy and light chain polypeptides. In such situations, the light chain should be placed before the heavy chain to avoid an excess of toxic free heavy chain (Proudfoot, Nature 322:52 (1986); Kohler, Proc. Natl. Acad. Sci. USA 77:2197 (1980)). The coding sequences for the heavy and light chains may comprise cDNA or genomic DNA.

Once an antibody molecule of the invention has been produced by an animal, chemically synthesized, or recombinantly expressed, it may be purified by any method known in the art for purification of an immunoglobulin molecule, for example, by chromatography (e.g., ion exchange, affinity, particularly by affinity for the specific antigen after Protein A, and sizing column chromatography), centrifugation, differential solubility, or by any other standard technique for the purification of proteins. In addition, the antibodies of the present invention or fragments thereof can be fused to heterologous polypeptide sequences described herein or otherwise known in the art, to facilitate purification.

The present invention encompasses antibodies recombinantly fused or chemically conjugated (including both covalently and non-covalently conjugations) to a polypeptide (or portion thereof, preferably at least 10, 20, 30, 40, 50, 60, 70, 80, 90 or 100 amino acids of the polypeptide) of the present invention to generate fusion proteins. The fusion does not necessarily need to be direct, but may occur through linker sequences. The antibodies may be specific for antigens other than polypeptides (or portion thereof, preferably at least 10, 20, 30, 40, 50, 60, 70, 80, 90 or 100 amino acids of the polypeptide) of the present invention. For example, antibodies may be used to target the polypeptides of the present invention to particular cell types, either in vitro or in vivo, by fusing or conjugating the polypeptides of the present invention to antibodies specific for particular cell surface receptors. Antibodies fused or conjugated to the polypeptides of the present invention may also be used in in vitro immunoassays and purification methods using methods known in the art. See e.g., Harbor et al., supra, and PCT publication WO 93/21232; EP 439,095; Naramura et al., Immunol. Lett. 39:91-99 (1994); U.S. Patent 5,474,981; Gillies et al., PNAS 89:1428-1432 (1992); Fell et al., J. Immunol. 146:2446-2452(1991), which are incorporated by reference in their entireties.

The present invention further includes compositions comprising the polypeptides of the present invention fused or conjugated to antibody domains other than the variable regions. For example, the polypeptides of the present invention may be fused or conjugated to an antibody Fc region, or portion thereof. The antibody portion fused to a polypeptide of the present invention may comprise the constant region, hinge region, CH1 domain, CH2 domain, and CH3 domain or any combination of whole domains or portions thereof. The polypeptides may also be fused or conjugated to the above antibody portions to form multimers. For example, Fc portions fused to the polypeptides of the present invention can form dimers through disulfide bonding between the Fc portions. Higher multimeric forms can be made by fusing the polypeptides to portions of IgA and IgM. Methods for fusing or conjugating the polypeptides of the present invention to antibody portions are known in the art. See, e.g., U.S. Patent Nos. 5,336,603; 5,622,929; 5,359,046; 5,349,053; 5,447,851; 5,112,946; EP 307,434; EP 367,166; PCT publications WO 96/04388; WO 91/06570; Ashkenazi et al., Proc. Natl. Acad. Sci. USA 88:10535-10539 (1991);

Zheng et al., J. Immunol. 154:5590-5600 (1995); and Vil et al., Proc. Natl. Acad. Sci. USA 89:11337- 11341(1992) (said references incorporated by reference in their entireties).

As discussed, supra, the polypeptides corresponding to a polypeptide, polypeptide fragment, or a variant of SEQ ID NO:Y may be fused or conjugated to the above antibody portions to increase the in vivo half life of the polypeptides or for use in immunoassays using methods known in the art. Further, the polypeptides corresponding to SEQ ID NO:Y may be fused or conjugated to the above antibody portions to facilitate purification. One reported example describes chimeric proteins consisting of the first two domains of the human CD4-polypeptide and various domains of the constant regions of the heavy or light chains of mammalian immunoglobulins. (EP 394,827; Traunecker et al., Nature 331:84-86 (1988). The polypeptides of the present invention fused or conjugated to an antibody having disulfide- linked dimeric structures (due to the IgG) may also be more efficient in binding and neutralizing other molecules, than the monomeric secreted protein or protein fragment alone. (Fountoulakis et al., J. Biochem. 270:3958-3964 (1995)). In many cases, the Fc part in a fusion protein is beneficial in therapy and diagnosis, and thus can result in, for example, improved pharmacokinetic properties. (EP A 232,262). Alternatively, deleting the Fc part after the fusion protein has been expressed, detected, and purified, would be desired. For example, the Fc portion may hinder therapy and diagnosis if the fusion protein is used as an antigen for immunizations. In drug discovery, for example, human proteins, such as hIL-5, have been fused with Fc portions for the purpose of high-throughput screening assays to identify antagonists of hIL-5. (See, Bennett et al., J. Molecular Recognition 8:52-58 (1995); Johanson et al., J. Biol. Chem. 270:9459-9471 (1995).

Moreover, the antibodies or fragments thereof of the present invention can be fused to marker sequences, such as a peptide to facilitate purification. In preferred embodiments, the marker amino acid sequence is a hexa-histidine peptide, such as the tag provided in a pQE vector (QIAGEN, Inc., 9259 Eton Avenue, Chatsworth, CA, 91311), among others, many of which are commercially available. As described in Gentz et al., Proc. Natl. Acad. Sci. USA 86:821-824 (1989), for instance, hexa-histidine provides for convenient purification of the fusion protein. Other peptide tags

useful for purification include, but are not limited to, the "HA" tag, which corresponds to an epitope derived from the influenza hemagglutinin protein (Wilson et al., Cell 37:767 (1984)) and the "flag" tag.

The present invention further encompasses antibodies or fragments thereof conjugated to a diagnostic or therapeutic agent. The antibodies can be used diagnostically to, for example, monitor the development or progression of a tumor as part of a clinical testing procedure to, e.g., determine the efficacy of a given treatment regimen. Detection can be facilitated by coupling the antibody to a detectable substance. Examples of detectable substances include various enzymes, prosthetic groups, fluorescent materials, luminescent materials, bioluminescent materials, radioactive materials, positron emitting metals using various positron emission tomographies, and nonradioactive paramagnetic metal ions. The detectable substance may be coupled or conjugated either directly to the antibody (or fragment thereof) or indirectly, through an intermediate (such as, for example, a linker known in the art) using techniques known in the art. See, for example, U.S. Patent No. 4,741,900 for metal ions which can be conjugated to antibodies for use as diagnostics according to the present invention. Examples of suitable enzymes include horseradish peroxidase, alkaline phosphatase, beta-galactosidase, or acetylcholinesterase; examples of suitable prosthetic group complexes include streptavidin/biotin and avidin/biotin; examples of suitable fluorescent materials include umbelliferone, fluorescein, fluorescein isothiocyanate, rhodamine, dichlorotriazinylamine fluorescein, dansyl chloride or phycoerythrin; an example of a luminescent material includes luminol; examples of bioluminescent materials include luciferase, luciferin, and aequorin; and examples of suitable radioactive material include 125I, 131I, 111In or 99Tc.

Further, an antibody or fragment thereof may be conjugated to a therapeutic moiety such as a cytotoxin, e.g., a cytostatic or cytocidal agent, a therapeutic agent or a radioactive metal ion, e.g., alpha-emitters such as, for example, 213Bi. A cytotoxin or cytotoxic agent includes any agent that is detrimental to cells. Examples include paclitaxol, cytochalasin B, gramicidin D, ethidium bromide, emetine, mitomycin, etoposide, tenoposide, vincristine, vinblastine, colchicin, doxorubicin, daunorubicin, dihydroxy anthracin dione, mitoxantrone, mithramycin, actinomycin D, 1-

dehydrotestosterone, glucocorticoids, procaine, tetracaine, lidocaine, propranolol, and puromycin and analogs or homologs thereof. Therapeutic agents include, but are not limited to, antimetabolites (e.g., methotrexate, 6-mercaptopurine, 6-thioguanine, cytarabine, 5-fluorouracil decarbazine), alkylating agents (e.g., mechlorethamine, thioepa chlorambucil, melphalan, carmustine (BSNU) and lomustine (CCNU), cyclothosphamide, busulfan, dibromomannitol, streptozotocin, mitomycin C, and cis-dichlorodiamine platinum (II) (DDP) cisplatin), anthracyclines (e.g., daunorubicin (formerly daunomycin) and doxorubicin), antibiotics (e.g., dactinomycin (formerly actinomycin), bleomycin, mithramycin, and anthramycin (AMC)), and anti-mitotic agents (e.g., vincristine and vinblastine).

The conjugates of the invention can be used for modifying a given biological response, the therapeutic agent or drug moiety is not to be construed as limited to classical chemical therapeutic agents. For example, the drug moiety may be a protein or polypeptide possessing a desired biological activity. Such proteins may include, for example, a toxin such as abrin, ricin A, pseudomonas exotoxin, or diphtheria toxin; a protein such as tumor necrosis factor, a-interferon, ß-interferon, nerve growth factor, platelet derived growth factor, tissue plasminogen activator, an apoptotic agent, e.g., TNF-alpha, TNF-beta, AIM I (See, International Publication No. WO 97/33899), AIM II (See, International Publication No. WO 97/34911), Fas Ligand (Takahashi *et al., Int. Immunol., 6*:1567-1574 (1994)), VEGI (See, International Publication No. WO 99/23105), a thrombotic agent or an anti- angiogenic agent, e.g., angiostatin or endostatin; or, biological response modifiers such as, for example, lymphokines, interleukin-1 ("IL-1"), interleukin-2 ("IL-2"), interleukin-6 ("IL-6"), granulocyte macrophage colony stimulating factor ("GM-CSF"), granulocyte colony stimulating factor ("G-CSF"), or other growth factors.

Antibodies may also be attached to solid supports, which are particularly useful for immunoassays or purification of the target antigen. Such solid supports include, but are not limited to, glass, cellulose, polyacrylamide, nylon, polystyrene, polyvinyl chloride or polypropylene.

Techniques for conjugating such therapeutic moiety to antibodies are well known, see, e.g., Arnon et al., "Monoclonal Antibodies For Immunotargeting Of Drugs In Cancer Therapy", in Monoclonal Antibodies And Cancer Therapy, Reisfeld

et al. (eds.), pp. 243-56 (Alan R. Liss, Inc. 1985); Hellstrom et al., "Antibodies For Drug Delivery", in Controlled Drug Delivery (2nd Ed.), Robinson et al. (eds.), pp. 623-53 (Marcel Dekker, Inc. 1987); Thorpe, "Antibody Carriers Of Cytotoxic Agents In Cancer Therapy: A Review", in Monoclonal Antibodies '84: Biological And Clinical Applications, Pinchera et al. (eds.), pp. 475-506 (1985); "Analysis, Results, And Future Prospective Of The Therapeutic Use Of Radiolabeled Antibody In Cancer Therapy", in Monoclonal Antibodies For Cancer Detection And Therapy, Baldwin et al. (eds.), pp. 303-16 (Academic Press 1985), and Thorpe et al., "The Preparation And Cytotoxic Properties Of Antibody-Toxin Conjugates", Immunol. Rev. 62:119-58 (1982).

Alternatively, an antibody can be conjugated to a second antibody to form an antibody heteroconjugate as described by Segal in U.S. Patent No. 4,676,980, which is incorporated herein by reference in its entirety.

An antibody, with or without a therapeutic moiety conjugated to it, administered alone or in combination with cytotoxic factor(s) and/or cytokine(s) can be used as a therapeutic.

Immunophenotyping

The antibodies of the invention may be utilized for immunophenotyping of cell lines and biological samples. The translation product of the gene of the present invention may be useful as a cell specific marker, or more specifically as a cellular marker that is differentially expressed at various stages of differentiation and/or maturation of particular cell types. Monoclonal antibodies directed against a specific epitope, or combination of epitopes, will allow for the screening of cellular populations expressing the marker. Various techniques can be utilized using monoclonal antibodies to screen for cellular populations expressing the marker(s), and include magnetic separation using antibody-coated magnetic beads, "panning" with antibody attached to a solid matrix (i.e., plate), and flow cytometry (See, e.g., U.S. Patent 5,985,660; and Morrison *et al., Cell, 96*:737-49 (1999)).

These techniques allow for the screening of particular populations of cells, such as might be found with hematological malignancies (i.e. minimal residual disease (MRD) in acute leukemic patients) and "non-self" cells in transplantations to

prevent Graft-versus-Host Disease (GVHD). Alternatively, these techniques allow for the screening of hematopoietic stem and progenitor cells capable of undergoing proliferation and/or differentiation, as might be found in human umbilical cord blood.

Assays For Antibody Binding

The antibodies of the invention may be assayed for immunospecific binding by any method known in the art. The immunoassays which can be used include but are not limited to competitive and non-competitive assay systems using techniques such as western blots, radioimmunoassays, ELISA (enzyme linked immunosorbent assay), "sandwich" immunoassays, immunoprecipitation assays, precipitin reactions, gel diffusion precipitin reactions, immunodiffusion assays, agglutination assays, complement-fixation assays, immunoradiometric assays, fluorescent immunoassays, protein A immunoassays, to name but a few. Such assays are routine and well known in the art (see, e.g., Ausubel et al, eds, 1994, Current Protocols in Molecular Biology, Vol. 1, John Wiley & Sons, Inc., New York, which is incorporated by reference herein in its entirety). Exemplary immunoassays are described briefly below (but are not intended by way of limitation).

Immunoprecipitation protocols generally comprise lysing a population of cells in a lysis buffer such as RIPA buffer (1% NP-40 or Triton X- 100, 1% sodium deoxycholate, 0.1% SDS, 0.15 M NaCl, 0.01 M sodium phosphate at pH 7.2, 1% Trasylol) supplemented with protein phosphatase and/or protease inhibitors (e.g., EDTA, PMSF, aprotinin, sodium vanadate), adding the antibody of interest to the cell lysate, incubating for a period of time (e.g., 1-4 hours) at 4° C, adding protein A and/or protein G sepharose beads to the cell lysate, incubating for about an hour or more at 4° C, washing the beads in lysis buffer and resuspending the beads in SDS/sample buffer. The ability of the antibody of interest to immunoprecipitate a particular antigen can be assessed by, e.g., western blot analysis. One of skill in the art would be knowledgeable as to the parameters that can be modified to increase the binding of the antibody to an antigen and decrease the background (e.g., pre-clearing the cell lysate with sepharose beads). For further discussion regarding immunoprecipitation protocols see, e.g., Ausubel et al, eds, 1994, Current Protocols in Molecular Biology, Vol. 1, John Wiley & Sons, Inc., New York at 10.16.1.

Western blot analysis generally comprises preparing protein samples, electrophoresis of the protein samples in a polyacrylamide gel (e.g., 8%- 20% SDS-PAGE depending on the molecular weight of the antigen), transferring the protein sample from the polyacrylamide gel to a membrane such as nitrocellulose, PVDF or nylon, blocking the membrane in blocking solution (e.g., PBS with 3% BSA or non-fat milk), washing the membrane in washing buffer (e.g., PBS-Tween 20), blocking the membrane with primary antibody (the antibody of interest) diluted in blocking buffer, washing the membrane in washing buffer, blocking the membrane with a secondary antibody (which recognizes the primary antibody, e.g., an anti-human antibody) conjugated to an enzymatic substrate (e.g., horseradish peroxidase or alkaline phosphatase) or radioactive molecule (e.g., 32P or 125I) diluted in blocking buffer, washing the membrane in wash buffer, and detecting the presence of the antigen. One of skill in the art would be knowledgeable as to the parameters that can be modified to increase the signal detected and to reduce the background noise. For further discussion regarding western blot protocols see, e.g., Ausubel et al, eds, 1994, Current Protocols in Molecular Biology, Vol. 1, John Wiley & Sons, Inc., New York at 10.8.1.

ELISAs comprise preparing antigen, coating the well of a 96 well microtiter plate with the antigen, adding the antibody of interest conjugated to a detectable compound such as an enzymatic substrate (e.g., horseradish peroxidase or alkaline phosphatase) to the well and incubating for a period of time, and detecting the presence of the antigen. In ELISAs the antibody of interest does not have to be conjugated to a detectable compound; instead, a second antibody (which recognizes the antibody of interest) conjugated to a detectable compound may be added to the well. Further, instead of coating the well with the antigen, the antibody may be coated to the well. In this case, a second antibody conjugated to a detectable compound may be added following the addition of the antigen of interest to the coated well. One of skill in the art would be knowledgeable as to the parameters that can be modified to increase the signal detected as well as other variations of ELISAs known in the art. For further discussion regarding ELISAs see, e.g., Ausubel et al, eds, 1994, Current Protocols in Molecular Biology, Vol. 1, John Wiley & Sons, Inc., New York at 11.2.1.

The binding affinity of an antibody to an antigen and the off-rate of an antibody-antigen interaction can be determined by competitive binding assays. One example of a competitive binding assay is a radioimmunoassay comprising the incubation of labeled antigen (e.g., 3H or 125I) with the antibody of interest in the presence of increasing amounts of unlabeled antigen, and the detection of the antibody bound to the labeled antigen. The affinity of the antibody of interest for a particular antigen and the binding off-rates can be determined from the data by scatchard plot analysis. Competition with a second antibody can also be determined using radioimmunoassays. In this case, the antigen is incubated with antibody of interest conjugated to a labeled compound (e.g., 3H or 125I) in the presence of increasing amounts of an unlabeled second antibody.

Therapeutic Uses

The present invention is further directed to antibody-based therapies which involve administering antibodies of the invention to an animal, preferably a mammal, and most preferably a human, patient for treating one or more of the disclosed diseases, disorders, or conditions. Therapeutic compounds of the invention include, but are not limited to, antibodies of the invention (including fragments, analogs and derivatives thereof as described herein) and nucleic acids encoding antibodies of the invention (including fragments, analogs and derivatives thereof and anti-idiotypic antibodies as described herein). The antibodies of the invention can be used to treat, inhibit or prevent diseases, disorders or conditions associated with aberrant expression and/or activity of a polypeptide of the invention, including, but not limited to, any one or more of the diseases, disorders, or conditions described herein. The treatment and/or prevention of diseases, disorders, or conditions associated with aberrant expression and/or activity of a polypeptide of the invention includes, but is not limited to, alleviating symptoms associated with those diseases, disorders or conditions. Antibodies of the invention may be provided in pharmaceutically acceptable compositions as known in the art or as described herein.

A summary of the ways in which the antibodies of the present invention may be used therapeutically includes binding polynucleotides or polypeptides of the present invention locally or systemically in the body or by direct cytotoxicity of the

antibody, e.g. as mediated by complement (CDC) or by effector cells (ADCC). Some of these approaches are described in more detail below. Armed with the teachings provided herein, one of ordinary skill in the art will know how to use the antibodies of the present invention for diagnostic, monitoring or therapeutic purposes without undue experimentation.

The antibodies of this invention may be advantageously utilized in combination with other monoclonal or chimeric antibodies, or with lymphokines or hematopoietic growth factors (such as, e.g., IL-2, IL-3 and IL-7), for example, which serve to increase the number or activity of effector cells which interact with the antibodies.

The antibodies of the invention may be administered alone or in combination with other types of treatments (e.g., radiation therapy, chemotherapy, hormonal therapy, immunotherapy and anti-tumor agents). Generally, administration of products of a species origin or species reactivity (in the case of antibodies) that is the same species as that of the patient is preferred. Thus, in a preferred embodiment, human antibodies, fragments derivatives, analogs, or nucleic acids, are administered to a human patient for therapy or prophylaxis.

It is preferred to use high affinity and/or potent in vivo inhibiting and/or neutralizing antibodies against polypeptides or polynucleotides of the present invention, fragments or regions thereof, for both immunoassays directed to and therapy of disorders related to polynucleotides or polypeptides, including fragments thereof, of the present invention. Such antibodies, fragments, or regions, will preferably have an affinity for polynucleotides or polypeptides of the invention, including fragments thereof. Preferred binding affinities include those with a dissociation constant or Kd less than 5 X 10^{-2} M, 10^{-2} M, 5 X 10^{-3} M, 10^{-3} M, 5 X 10^{-4} M, 10^{-4} M, 5 X 10^{-5} M, 10^{-5} M, 5 X 10^{-6} M, 10^{-6} M, 5 X 10^{-7} M, 10^{-7} M, 5 X 10^{-8} M, 10^{-8} M, 5 X 10^{-9} M, 10^{-9} M, 5 X 10^{-10} M, 10^{-10} M, 5 X 10^{-11} M, 10^{-11} M, 5 X 10^{-12} M, 10^{-12} M, 5 X 10^{-13} M, 10^{-13} M, 5 X 10^{-14} M, 10^{-14} M, 5 X 10^{-15} M, and 10^{-15} M.

Gene Therapy

In a specific embodiment, nucleic acids comprising sequences encoding antibodies or functional derivatives thereof, are administered to treat, inhibit or

prevent a disease or disorder associated with aberrant expression and/or activity of a polypeptide of the invention, by way of gene therapy. Gene therapy refers to therapy performed by the administration to a subject of an expressed or expressible nucleic acid. In this embodiment of the invention, the nucleic acids produce their encoded protein that mediates a therapeutic effect.

Any of the methods for gene therapy available in the art can be used according to the present invention. Exemplary methods are described below.

For general reviews of the methods of gene therapy, see Goldspiel et al., Clinical Pharmacy 12:488-505 (1993); Wu and Wu, Biotherapy 3:87-95 (1991); Tolstoshev, Ann. Rev. Pharmacol. Toxicol. 32:573-596 (1993); Mulligan, Science 260:926-932 (1993); and Morgan and Anderson, Ann. Rev. Biochem. 62:191-217 (1993); May, TIBTECH 11(5):155-215 (1993). Methods commonly known in the art of recombinant DNA technology which can be used are described in Ausubel et al. (eds.), Current Protocols in Molecular Biology, John Wiley & Sons, NY (1993); and Kriegler, Gene Transfer and Expression, A Laboratory Manual, Stockton Press, NY (1990).

In a preferred aspect, the compound comprises nucleic acid sequences encoding an antibody, said nucleic acid sequences being part of expression vectors that express the antibody or fragments or chimeric proteins or heavy or light chains thereof in a suitable host. In particular, such nucleic acid sequences have promoters operably linked to the antibody coding region, said promoter being inducible or constitutive, and, optionally, tissue- specific. In another particular embodiment, nucleic acid molecules are used in which the antibody coding sequences and any other desired sequences are flanked by regions that promote homologous recombination at a desired site in the genome, thus providing for intrachromosomal expression of the antibody encoding nucleic acids (Koller and Smithies, Proc. Natl. Acad. Sci. USA 86:8932-8935 (1989); Zijlstra et al., Nature 342:435-438 (1989). In specific embodiments, the expressed antibody molecule is a single chain antibody; alternatively, the nucleic acid sequences include sequences encoding both the heavy and light chains, or fragments thereof, of the antibody.

Delivery of the nucleic acids into a patient may be either direct, in which case the patient is directly exposed to the nucleic acid or nucleic acid- carrying vectors, or

indirect, in which case, cells are first transformed with the nucleic acids in vitro, then transplanted into the patient. These two approaches are known, respectively, as in vivo or ex vivo gene therapy.

In a specific embodiment, the nucleic acid sequences are directly administered in vivo, where it is expressed to produce the encoded product. This can be accomplished by any of numerous methods known in the art, e.g., by constructing them as part of an appropriate nucleic acid expression vector and administering it so that they become intracellular, e.g., by infection using defective or attenuated retrovirals or other viral vectors (see U.S. Patent No. 4,980,286), or by direct injection of naked DNA, or by use of microparticle bombardment (e.g., a gene gun; Biolistic, Dupont), or coating with lipids or cell-surface receptors or transfecting agents, encapsulation in liposomes, microparticles, or microcapsules, or by administering them in linkage to a peptide which is known to enter the nucleus, by administering it in linkage to a ligand subject to receptor-mediated endocytosis (see, e.g., Wu and Wu, J. Biol. Chem. 262:4429-4432 (1987)) (which can be used to target cell types specifically expressing the receptors), etc. In another embodiment, nucleic acid-ligand complexes can be formed in which the ligand comprises a fusogenic viral peptide to disrupt endosomes, allowing the nucleic acid to avoid lysosomal degradation. In yet another embodiment, the nucleic acid can be targeted in vivo for cell specific uptake and expression, by targeting a specific receptor (see, e.g., PCT Publications WO 92/06180; WO 92/22635; WO92/20316; WO93/14188, WO 93/20221). Alternatively, the nucleic acid can be introduced intracellularly and incorporated within host cell DNA for expression, by homologous recombination (Koller and Smithies, Proc. Natl. Acad. Sci. USA 86:8932-8935 (1989); Zijlstra et al., Nature 342:435-438 (1989)).

In a specific embodiment, viral vectors that contains nucleic acid sequences encoding an antibody of the invention are used. For example, a retroviral vector can be used (see Miller et al., Meth. Enzymol. 217:581-599 (1993)). These retroviral vectors contain the components necessary for the correct packaging of the viral genome and integration into the host cell DNA. The nucleic acid sequences encoding the antibody to be used in gene therapy are cloned into one or more vectors, which facilitates delivery of the gene into a patient. More detail about retroviral vectors can

be found in Boesen et al., Biotherapy 6:291-302 (1994), which describes the use of a retroviral vector to deliver the mdr1 gene to hematopoietic stem cells in order to make the stem cells more resistant to chemotherapy. Other references illustrating the use of retroviral vectors in gene therapy are: Clowes et al., J. Clin. Invest. 93:644-651 (1994); Kiem et al., Blood 83:1467-1473 (1994); Salmons and Gunzberg, Human Gene Therapy 4:129-141 (1993); and Grossman and Wilson, Curr. Opin. in Genetics and Devel. 3:110-114 (1993).

Adenoviruses are other viral vectors that can be used in gene therapy. Adenoviruses are especially attractive vehicles for delivering genes to respiratory epithelia. Adenoviruses naturally infect respiratory epithelia where they cause a mild disease. Other targets for adenovirus-based delivery systems are liver, the central nervous system, endothelial cells, and muscle. Adenoviruses have the advantage of being capable of infecting non-dividing cells. Kozarsky and Wilson, Current Opinion in Genetics and Development 3:499-503 (1993) present a review of adenovirus-based gene therapy. Bout et al., Human Gene Therapy 5:3-10 (1994) demonstrated the use of adenovirus vectors to transfer genes to the respiratory epithelia of rhesus monkeys. Other instances of the use of adenoviruses in gene therapy can be found in Rosenfeld et al., Science 252:431-434 (1991); Rosenfeld et al., Cell 68:143- 155 (1992); Mastrangeli et al., J. Clin. Invest. 91:225-234 (1993); PCT Publication WO94/12649; and Wang, et al., Gene Therapy 2:775-783 (1995). In a preferred embodiment, adenovirus vectors are used.

Adeno-associated virus (AAV) has also been proposed for use in gene therapy (Walsh et al., Proc. Soc. Exp. Biol. Med. 204:289-300 (1993); U.S. Patent No. 5,436,146).

Another approach to gene therapy involves transferring a gene to cells in tissue culture by such methods as electroporation, lipofection, calcium phosphate mediated transfection, or viral infection. Usually, the method of transfer includes the transfer of a selectable marker to the cells. The cells are then placed under selection to isolate those cells that have taken up and are expressing the transferred gene. Those cells are then delivered to a patient.

In this embodiment, the nucleic acid is introduced into a cell prior to administration in vivo of the resulting recombinant cell. Such introduction can be

carried out by any method known in the art, including but not limited to transfection, electroporation, microinjection, infection with a viral or bacteriophage vector containing the nucleic acid sequences, cell fusion, chromosome-mediated gene transfer, microcell-mediated gene transfer, spheroplast fusion, etc. Numerous techniques are known in the art for the introduction of foreign genes into cells (see, e.g., Loeffler and Behr, Meth. Enzymol. 217:599-618 (1993); Cohen et al., Meth. Enzymol. 217:618-644 (1993); Cline, Pharmac. Ther. 29:69-92m (1985) and may be used in accordance with the present invention, provided that the necessary developmental and physiological functions of the recipient cells are not disrupted. The technique should provide for the stable transfer of the nucleic acid to the cell, so that the nucleic acid is expressible by the cell and preferably heritable and expressible by its cell progeny.

The resulting recombinant cells can be delivered to a patient by various methods known in the art. Recombinant blood cells (e.g., hematopoietic stem or progenitor cells) are preferably administered intravenously. The amount of cells envisioned for use depends on the desired effect, patient state, etc., and can be determined by one skilled in the art.

Cells into which a nucleic acid can be introduced for purposes of gene therapy encompass any desired, available cell type, and include but are not limited to epithelial cells, endothelial cells, keratinocytes, fibroblasts, muscle cells, hepatocytes; blood cells such as Tlymphocytes, Blymphocytes, monocytes, macrophages, neutrophils, eosinophils, megakaryocytes, granulocytes; various stem or progenitor cells, in particular hematopoietic stem or progenitor cells, e.g., as obtained from bone marrow, umbilical cord blood, peripheral blood, fetal liver, etc.

In a preferred embodiment, the cell used for gene therapy is autologous to the patient.

In an embodiment in which recombinant cells are used in gene therapy, nucleic acid sequences encoding an antibody are introduced into the cells such that they are expressible by the cells or their progeny, and the recombinant cells are then administered in vivo for therapeutic effect. In a specific embodiment, stem or progenitor cells are used. Any stem and/or progenitor cells which can be isolated and maintained in vitro can potentially be used in accordance with this embodiment of

the present invention (see e.g. PCT Publication WO 94/08598; Stemple and Anderson, Cell 71:973-985 (1992); Rheinwald, Meth. Cell Bio. 21A:229 (1980); and Pittelkow and Scott, Mayo Clinic Proc. 61:771 (1986)).

In a specific embodiment, the nucleic acid to be introduced for purposes of gene therapy comprises an inducible promoter operably linked to the coding region, such that expression of the nucleic acid is controllable by controlling the presence or absence of the appropriate inducer of transcription.

Demonstration of Therapeutic or Prophylactic Activity

The compounds or pharmaceutical compositions of the invention are preferably tested in vitro, and then in vivo for the desired therapeutic or prophylactic activity, prior to use in humans. For example, in vitro assays to demonstrate the therapeutic or prophylactic utility of a compound or pharmaceutical composition include, the effect of a compound on a cell line or a patient tissue sample. The effect of the compound or composition on the cell line and/or tissue sample can be determined utilizing techniques known to those of skill in the art including, but not limited to, rosette formation assays and cell lysis assays. In accordance with the invention, in vitro assays which can be used to determine whether administration of a specific compound is indicated, include in vitro cell culture assays in which a patient tissue sample is grown in culture, and exposed to or otherwise administered a compound, and the effect of such compound upon the tissue sample is observed.

Therapeutic/Prophylactic Administration and Composition

The invention provides methods of treatment, inhibition and prophylaxis by administration to a subject of an effective amount of a compound or pharmaceutical composition of the invention, preferably an antibody of the invention. In a preferred aspect, the compound is substantially purified (e.g., substantially free from substances that limit its effect or produce undesired side-effects). The subject is preferably an animal, including but not limited to animals such as cows, pigs, horses, chickens, cats, dogs, etc., and is preferably a mammal, and most preferably human.

Formulations and methods of administration that can be employed when the compound comprises a nucleic acid or an immunoglobulin are described above;

additional appropriate formulations and routes of administration can be selected from among those described herein below.

Various delivery systems are known and can be used to administer a compound of the invention, e.g., encapsulation in liposomes, microparticles, microcapsules, recombinant cells capable of expressing the compound, receptor-mediated endocytosis (see, e.g., Wu and Wu, J. Biol. Chem. 262:4429-4432 (1987)), construction of a nucleic acid as part of a retroviral or other vector, etc. Methods of introduction include but are not limited to intradermal, intramuscular, intraperitoneal, intravenous, subcutaneous, intranasal, epidural, and oral routes. The compounds or compositions may be administered by any convenient route, for example by infusion or bolus injection, by absorption through epithelial or mucocutaneous linings (e.g., oral mucosa, rectal and intestinal mucosa, etc.) and may be administered together with other biologically active agents. Administration can be systemic or local. In addition, it may be desirable to introduce the pharmaceutical compounds or compositions of the invention into the central nervous system by any suitable route, including intraventricular and intrathecal injection; intraventricular injection may be facilitated by an intraventricular catheter, for example, attached to a reservoir, such as an Ommaya reservoir. Pulmonary administration can also be employed, e.g., by use of an inhaler or nebulizer, and formulation with an aerosolizing agent.

In a specific embodiment, it may be desirable to administer the pharmaceutical compounds or compositions of the invention locally to the area in need of treatment; this may be achieved by, for example, and not by way of limitation, local infusion during surgery, topical application, e.g., in conjunction with a wound dressing after surgery, by injection, by means of a catheter, by means of a suppository, or by means of an implant, said implant being of a porous, non-porous, or gelatinous material, including membranes, such as sialastic membranes, or fibers. Preferably, when administering a protein, including an antibody, of the invention, care must be taken to use materials to which the protein does not absorb.

In another embodiment, the compound or composition can be delivered in a vesicle, in particular a liposome (see Langer, Science 249:1527-1533 (1990); Treat et al., in Liposomes in the Therapy of Infectious Disease and Cancer, Lopez-Berestein

and Fidler (eds.), Liss, New York, pp. 353- 365 (1989); Lopez-Berestein, ibid., pp. 317-327; see generally ibid.)

In yet another embodiment, the compound or composition can be delivered in a controlled release system. In one embodiment, a pump may be used (see Langer, supra; Sefton, CRC Crit. Ref. Biomed. Eng. 14:201 (1987); Buchwald et al., Surgery 88:507 (1980); Saudek et al., N. Engl. J. Med. 321:574 (1989)). In another embodiment, polymeric materials can be used (see Medical Applications of Controlled Release, Langer and Wise (eds.), CRC Pres., Boca Raton, Florida (1974); Controlled Drug Bioavailability, Drug Product Design and Performance, Smolen and Ball (eds.), Wiley, New York (1984); Ranger and Peppas, J., Macromol. Sci. Rev. Macromol. Chem. 23:61 (1983); see also Levy et al., Science 228:190 (1985); During et al., Ann. Neurol. 25:351 (1989); Howard et al., J.Neurosurg. 71:105 (1989)). In yet another embodiment, a controlled release system can be placed in proximity of the therapeutic target, i.e., the brain, thus requiring only a fraction of the systemic dose (see, e.g., Goodson, in Medical Applications of Controlled Release, supra, vol. 2, pp. 115-138 (1984)).

Other controlled release systems are discussed in the review by Langer (Science 249:1527-1533 (1990)).

In a specific embodiment where the compound of the invention is a nucleic acid encoding a protein, the nucleic acid can be administered in vivo to promote expression of its encoded protein, by constructing it as part of an appropriate nucleic acid expression vector and administering it so that it becomes intracellular, e.g., by use of a retroviral vector (see U.S. Patent No. 4,980,286), or by direct injection, or by use of microparticle bombardment (e.g., a gene gun; Biolistic, Dupont), or coating with lipids or cell-surface receptors or transfecting agents, or by administering it in linkage to a homeobox- like peptide which is known to enter the nucleus (see e.g., Joliot et al., Proc. Natl. Acad. Sci. USA 88:1864-1868 (1991)), etc. Alternatively, a nucleic acid can be introduced intracellularly and incorporated within host cell DNA for expression, by homologous recombination.

The present invention also provides pharmaceutical compositions. Such compositions comprise a therapeutically effective amount of a compound, and a pharmaceutically acceptable carrier. In a specific embodiment, the term

"pharmaceutically acceptable" means approved by a regulatory agency of the Federal or a state government or listed in the U.S. Pharmacopeia or other generally recognized pharmacopeia for use in animals, and more particularly in humans. The term "carrier" refers to a diluent, adjuvant, excipient, or vehicle with which the therapeutic is administered. Such pharmaceutical carriers can be sterile liquids, such as water and oils, including those of petroleum, animal, vegetable or synthetic origin, such as peanut oil, soybean oil, mineral oil, sesame oil and the like. Water is a preferred carrier when the pharmaceutical composition is administered intravenously. Saline solutions and aqueous dextrose and glycerol solutions can also be employed as liquid carriers, particularly for injectable solutions. Suitable pharmaceutical excipients include starch, glucose, lactose, sucrose, gelatin, malt, rice, flour, chalk, silica gel, sodium stearate, glycerol monostearate, talc, sodium chloride, dried skim milk, glycerol, propylene, glycol, water, ethanol and the like. The composition, if desired, can also contain minor amounts of wetting or emulsifying agents, or pH buffering agents. These compositions can take the form of solutions, suspensions, emulsion, tablets, pills, capsules, powders, sustained-release formulations and the like. The composition can be formulated as a suppository, with traditional binders and carriers such as triglycerides. Oral formulation can include standard carriers such as pharmaceutical grades of mannitol, lactose, starch, magnesium stearate, sodium saccharine, cellulose, magnesium carbonate, etc. Examples of suitable pharmaceutical carriers are described in "Remington's Pharmaceutical Sciences" by E.W. Martin. Such compositions will contain a therapeutically effective amount of the compound, preferably in purified form, together with a suitable amount of carrier so as to provide the form for proper administration to the patient. The formulation should suit the mode of administration.

In a preferred embodiment, the composition is formulated in accordance with routine procedures as a pharmaceutical composition adapted for intravenous administration to human beings. Typically, compositions for intravenous administration are solutions in sterile isotonic aqueous buffer. Where necessary, the composition may also include a solubilizing agent and a local anesthetic such as lignocaine to ease pain at the site of the injection. Generally, the ingredients are supplied either separately or mixed together in unit dosage form, for example, as a dry

lyophilized powder or water free concentrate in a hermetically sealed container such as an ampoule or sachette indicating the quantity of active agent. Where the composition is to be administered by infusion, it can be dispensed with an infusion bottle containing sterile pharmaceutical grade water or saline. Where the composition is administered by injection, an ampoule of sterile water for injection or saline can be provided so that the ingredients may be mixed prior to administration.

The compounds of the invention can be formulated as neutral or salt forms. Pharmaceutically acceptable salts include those formed with anions such as those derived from hydrochloric, phosphoric, acetic, oxalic, tartaric acids, etc., and those formed with cations such as those derived from sodium, potassium, ammonium, calcium, ferric hydroxides, isopropylamine, triethylamine, 2-ethylamino ethanol, histidine, procaine, etc.

The amount of the compound of the invention which will be effective in the treatment, inhibition and prevention of a disease or disorder associated with aberrant expression and/or activity of a polypeptide of the invention can be determined by standard clinical techniques. In addition, in vitro assays may optionally be employed to help identify optimal dosage ranges. The precise dose to be employed in the formulation will also depend on the route of administration, and the seriousness of the disease or disorder, and should be decided according to the judgment of the practitioner and each patient's circumstances. Effective doses may be extrapolated from dose-response curves derived from in vitro or animal model test systems.

For antibodies, the dosage administered to a patient is typically 0.1 mg/kg to 100 mg/kg of the patient's body weight. Preferably, the dosage administered to a patient is between 0.1 mg/kg and 20 mg/kg of the patient's body weight, more preferably 1 mg/kg to 10 mg/kg of the patient's body weight. Generally, human antibodies have a longer half-life within the human body than antibodies from other species due to the immune response to the foreign polypeptides. Thus, lower dosages of human antibodies and less frequent administration is often possible. Further, the dosage and frequency of administration of antibodies of the invention may be reduced by enhancing uptake and tissue penetration (e.g., into the brain) of the antibodies by modifications such as, for example, lipidation.

The invention also provides a pharmaceutical pack or kit comprising one or more containers filled with one or more of the ingredients of the pharmaceutical compositions of the invention. Optionally associated with such container(s) can be a notice in the form prescribed by a governmental agency regulating the manufacture, use or sale of pharmaceuticals or biological products, which notice reflects approval by the agency of manufacture, use or sale for human administration.

Diagnosis and Imaging

Labeled antibodies, and derivatives and analogs thereof, which specifically bind to a polypeptide of interest can be used for diagnostic purposes to detect, diagnose, or monitor diseases, disorders, and/or conditions associated with the aberrant expression and/or activity of a polypeptide of the invention. The invention provides for the detection of aberrant expression of a polypeptide of interest, comprising (a) assaying the expression of the polypeptide of interest in cells or body fluid of an individual using one or more antibodies specific to the polypeptide interest and (b) comparing the level of gene expression with a standard gene expression level, whereby an increase or decrease in the assayed polypeptide gene expression level compared to the standard expression level is indicative of aberrant expression.

The invention provides a diagnostic assay for diagnosing a disorder, comprising (a) assaying the expression of the polypeptide of interest in cells or body fluid of an individual using one or more antibodies specific to the polypeptide interest and (b) comparing the level of gene expression with a standard gene expression level, whereby an increase or decrease in the assayed polypeptide gene expression level compared to the standard expression level is indicative of a particular disorder. With respect to cancer, the presence of a relatively high amount of transcript in biopsied tissue from an individual may indicate a predisposition for the development of the disease, or may provide a means for detecting the disease prior to the appearance of actual clinical symptoms. A more definitive diagnosis of this type may allow health professionals to employ preventative measures or aggressive treatment earlier thereby preventing the development or further progression of the cancer.

Antibodies of the invention can be used to assay protein levels in a biological sample using classical immunohistological methods known to those of skill in the art

(e.g., see Jalkanen, et al., J. Cell. Biol. 101:976-985 (1985); Jalkanen, et al., J. Cell . Biol. 105:3087-3096 (1987)). Other antibody-based methods useful for detecting protein gene expression include immunoassays, such as the enzyme linked immunosorbent assay (ELISA) and the radioimmunoassay (RIA). Suitable antibody assay labels are known in the art and include enzyme labels, such as, glucose oxidase; radioisotopes, such as iodine (125I, 121I), carbon (14C), sulfur (35S), tritium (3H), indium (112In), and technetium (99Tc); luminescent labels, such as luminol; and fluorescent labels, such as fluorescein and rhodamine, and biotin.

One aspect of the invention is the detection and diagnosis of a disease or disorder associated with aberrant expression of a polypeptide of interest in an animal, preferably a mammal and most preferably a human. In one embodiment, diagnosis comprises: a) administering (for example, parenterally, subcutaneously, or intraperitoneally) to a subject an effective amount of a labeled molecule which specifically binds to the polypeptide of interest; b) waiting for a time interval following the administering for permitting the labeled molecule to preferentially concentrate at sites in the subject where the polypeptide is expressed (and for unbound labeled molecule to be cleared to background level); c) determining background level; and d) detecting the labeled molecule in the subject, such that detection of labeled molecule above the background level indicates that the subject has a particular disease or disorder associated with aberrant expression of the polypeptide of interest. Background level can be determined by various methods including, comparing the amount of labeled molecule detected to a standard value previously determined for a particular system.

It will be understood in the art that the size of the subject and the imaging system used will determine the quantity of imaging moiety needed to produce diagnostic images. In the case of a radioisotope moiety, for a human subject, the quantity of radioactivity injected will normally range from about 5 to 20 millicuries of 99mTc. The labeled antibody or antibody fragment will then preferentially accumulate at the location of cells which contain the specific protein. In vivo tumor imaging is described in S.W. Burchiel et al., "Immunopharmacokinetics of Radiolabeled Antibodies and Their Fragments." (Chapter 13 in Tumor Imaging:

The Radiochemical Detection of Cancer, S.W. Burchiel and B. A. Rhodes, eds., Masson Publishing Inc. (1982).

Depending on several variables, including the type of label used and the mode of administration, the time interval following the administration for permitting the labeled molecule to preferentially concentrate at sites in the subject and for unbound labeled molecule to be cleared to background level is 6 to 48 hours or 6 to 24 hours or 6 to 12 hours. In another embodiment the time interval following administration is 5 to 20 days or 5 to 10 days.

In an embodiment, monitoring of the disease or disorder is carried out by repeating the method for diagnosing the disease or disease, for example, one month after initial diagnosis, six months after initial diagnosis, one year after initial diagnosis, etc.

Presence of the labeled molecule can be detected in the patient using methods known in the art for in vivo scanning. These methods depend upon the type of label used. Skilled artisans will be able to determine the appropriate method for detecting a particular label. Methods and devices that may be used in the diagnostic methods of the invention include, but are not limited to, computed tomography (CT), whole body scan such as position emission tomography (PET), magnetic resonance imaging (MRI), and sonography.

In a specific embodiment, the molecule is labeled with a radioisotope and is detected in the patient using a radiation responsive surgical instrument (Thurston et al., U.S. Patent No. 5,441,050). In another embodiment, the molecule is labeled with a fluorescent compound and is detected in the patient using a fluorescence responsive scanning instrument. In another embodiment, the molecule is labeled with a positron emitting metal and is detected in the patent using positron emission-tomography. In yet another embodiment, the molecule is labeled with a paramagnetic label and is detected in a patient using magnetic resonance imaging (MRI).

Kits

The present invention provides kits that can be used in the above methods. In one embodiment, a kit comprises an antibody of the invention, preferably a purified antibody, in one or more containers. In a specific embodiment, the kits of the present

invention contain a substantially isolated polypeptide comprising an epitope which is specifically immunoreactive with an antibody included in the kit. Preferably, the kits of the present invention further comprise a control antibody which does not react with the polypeptide of interest. In another specific embodiment, the kits of the present invention contain a means for detecting the binding of an antibody to a polypeptide of interest (e.g., the antibody may be conjugated to a detectable substrate such as a fluorescent compound, an enzymatic substrate, a radioactive compound or a luminescent compound, or a second antibody which recognizes the first antibody may be conjugated to a detectable substrate).

In another specific embodiment of the present invention, the kit is a diagnostic kit for use in screening serum containing antibodies specific against proliferative and/or cancerous polynucleotides and polypeptides. Such a kit may include a control antibody that does not react with the polypeptide of interest. Such a kit may include a substantially isolated polypeptide antigen comprising an epitope which is specifically immunoreactive with at least one anti-polypeptide antigen antibody. Further, such a kit includes means for detecting the binding of said antibody to the antigen (e.g., the antibody may be conjugated to a fluorescent compound such as fluorescein or rhodamine which can be detected by flow cytometry). In specific embodiments, the kit may include a recombinantly produced or chemically synthesized polypeptide antigen. The polypeptide antigen of the kit may also be attached to a solid support.

In a more specific embodiment the detecting means of the above-described kit includes a solid support to which said polypeptide antigen is attached. Such a kit may also include a non-attached reporter-labeled anti-human antibody. In this embodiment, binding of the antibody to the polypeptide antigen can be detected by binding of the said reporter-labeled antibody.

In an additional embodiment, the invention includes a diagnostic kit for use in screening serum containing antigens of the polypeptide of the invention. The diagnostic kit includes a substantially isolated antibody specifically immunoreactive with polypeptide or polynucleotide antigens, and means for detecting the binding of the polynucleotide or polypeptide antigen to the antibody. In one embodiment, the antibody is attached to a solid support. In a specific embodiment, the antibody may be a monoclonal antibody. The detecting means of the kit may include a second, labeled

monoclonal antibody. Alternatively, or in addition, the detecting means may include a labeled, competing antigen.

In one diagnostic configuration, test serum is reacted with a solid phase reagent having a surface-bound antigen obtained by the methods of the present invention. After binding with specific antigen antibody to the reagent and removing unbound serum components by washing, the reagent is reacted with reporter-labeled anti-human antibody to bind reporter to the reagent in proportion to the amount of bound anti-antigen antibody on the solid support. The reagent is again washed to remove unbound labeled antibody, and the amount of reporter associated with the reagent is determined. Typically, the reporter is an enzyme which is detected by incubating the solid phase in the presence of a suitable fluorometric, luminescent or colorimetric substrate (Sigma, St. Louis, MO).

The solid surface reagent in the above assay is prepared by known techniques for attaching protein material to solid support material, such as polymeric beads, dip sticks, 96-well plate or filter material. These attachment methods generally include non-specific adsorption of the protein to the support or covalent attachment of the protein, typically through a free amine group, to a chemically reactive group on the solid support, such as an activated carboxyl, hydroxyl, or aldehyde group. Alternatively, streptavidin coated plates can be used in conjunction with biotinylated antigen(s).

Thus, the invention provides an assay system or kit for carrying out this diagnostic method. The kit generally includes a support with surface- bound recombinant antigens, and a reporter-labeled anti-human antibody for detecting surface-bound anti-antigen antibody.

Fusion Proteins

Any polypeptide of the present invention can be used to generate fusion proteins. For example, the polypeptide of the present invention, when fused to a second protein, can be used as an antigenic tag. Antibodies raised against the polypeptide of the present invention can be used to indirectly detect the second protein by binding to the polypeptide. Moreover, because secreted proteins target

cellular locations based on trafficking signals, the polypeptides of the present invention can be used as targeting molecules once fused to other proteins.

Examples of domains that can be fused to polypeptides of the present invention include not only heterologous signal sequences, but also other heterologous functional regions. The fusion does not necessarily need to be direct, but may occur through linker sequences.

Moreover, fusion proteins may also be engineered to improve characteristics of the polypeptide of the present invention. For instance, a region of additional amino acids, particularly charged amino acids, may be added to the N-terminus of the polypeptide to improve stability and persistence during purification from the host cell or subsequent handling and storage. Also, peptide moieties may be added to the polypeptide to facilitate purification. Such regions may be removed prior to final preparation of the polypeptide. The addition of peptide moieties to facilitate handling of polypeptides are familiar and routine techniques in the art.

Moreover, polypeptides of the present invention, including fragments, and specifically epitopes, can be combined with parts of the constant domain of immunoglobulins (IgA, IgE, IgG, IgM) or portions thereof (CH1, CH2, CH3, and any combination thereof, including both entire domains and portions thereof), resulting in chimeric polypeptides. These fusion proteins facilitate purification and show an increased half-life in vivo. One reported example describes chimeric proteins consisting of the first two domains of the human CD4-polypeptide and various domains of the constant regions of the heavy or light chains of mammalian immunoglobulins. (EP A 394,827; Traunecker et al., Nature 331:84-86 (1988).) Fusion proteins having disulfide-linked dimeric structures (due to the IgG) can also be more efficient in binding and neutralizing other molecules, than the monomeric secreted protein or protein fragment alone. (Fountoulakis et al., J. Biochem. 270:3958-3964 (1995).) Polynucleotides comprising or alternatively consisting of nucleic acids which encode these fusion proteins are also encompassed by the invention.

Similarly, EP-A-O 464 533 (Canadian counterpart 2045869) discloses fusion proteins comprising various portions of constant region of immunoglobulin molecules together with another human protein or part thereof. In many cases, the Fc part in a

fusion protein is beneficial in therapy and diagnosis, and thus can result in, for example, improved pharmacokinetic properties. (EP-A 0232 262.) Alternatively, deleting the Fc part after the fusion protein has been expressed, detected, and purified, would be desired. For example, the Fc portion may hinder therapy and diagnosis if the fusion protein is used as an antigen for immunizations. In drug discovery, for example, human proteins, such as hIL-5, have been fused with Fc portions for the purpose of high-throughput screening assays to identify antagonists of hIL-5. (See, D. Bennett et al., J. Molecular Recognition 8:52-58 (1995); K. Johanson et al., J. Biol. Chem. 270:9459-9471 (1995).)

Moreover, the polypeptides of the present invention can be fused to marker sequences, such as a peptide which facilitates purification of the fused polypeptide. In preferred embodiments, the marker amino acid sequence is a hexa-histidine peptide, such as the tag provided in a pQE vector (QIAGEN, Inc., 9259 Eton Avenue, Chatsworth, CA, 91311), among others, many of which are commercially available. As described in Gentz et al., Proc. Natl. Acad. Sci. USA 86:821-824 (1989), for instance, hexa-histidine provides for convenient purification of the fusion protein. Another peptide tag useful for purification, the "HA" tag, corresponds to an epitope derived from the influenza hemagglutinin protein. (Wilson et al., Cell 37:767 (1984).)

Thus, any of these above fusions can be engineered using the polynucleotides or the polypeptides of the present invention.

Vectors, Host Cells, and Protein Production

The present invention also relates to vectors containing the polynucleotide of the present invention, host cells, and the production of polypeptides by recombinant techniques. The vector may be, for example, a phage, plasmid, viral, or retroviral vector. Retroviral vectors may be replication competent or replication defective. In the latter case, viral propagation generally will occur only in complementing host cells.

The polynucleotides may be joined to a vector containing a selectable marker for propagation in a host. Generally, a plasmid vector is introduced in a precipitate, such as a calcium phosphate precipitate, or in a complex with a charged lipid. If the

vector is a virus, it may be packaged in vitro using an appropriate packaging cell line and then transduced into host cells.

The polynucleotide insert should be operatively linked to an appropriate promoter, such as the phage lambda PL promoter, the E. coli lac, trp, phoA and tac promoters, the SV40 early and late promoters and promoters of retroviral LTRs, to name a few. Other suitable promoters will be known to the skilled artisan. The expression constructs will further contain sites for transcription initiation, termination, and, in the transcribed region, a ribosome binding site for translation. The coding portion of the transcripts expressed by the constructs will preferably include a translation initiating codon at the beginning and a termination codon (UAA, UGA or UAG) appropriately positioned at the end of the polypeptide to be translated.

As indicated, the expression vectors will preferably include at least one selectable marker. Such markers include dihydrofolate reductase, G418 or neomycin resistance for eukaryotic cell culture and tetracycline, kanamycin or ampicillin resistance genes for culturing in E. coli and other bacteria. Representative examples of appropriate hosts include, but are not limited to, bacterial cells, such as E. coli, Streptomyces and Salmonella typhimurium cells; fungal cells, such as yeast cells (e.g., Saccharomyces cerevisiae or Pichia pastoris (ATCC Accession No. 201178)); insect cells such as Drosophila S2 and Spodoptera Sf9 cells; animal cells such as CHO, COS, 293, and Bowes melanoma cells; and plant cells. Appropriate culture mediums and conditions for the above-described host cells are known in the art.

Among vectors preferred for use in bacteria include pQE70, pQE60 and pQE-9, available from QIAGEN, Inc.; pBluescript vectors, Phagescript vectors, pNH8A, pNH16a, pNH18A, pNH46A, available from Stratagene Cloning Systems, Inc.; and ptrc99a, pKK223-3, pKK233-3, pDR540, pRIT5 available from Pharmacia Biotech, Inc. Among preferred eukaryotic vectors are pWLNEO, pSV2CAT, pOG44, pXT1 and pSG available from Stratagene; and pSVK3, pBPV, pMSG and pSVL available from Pharmacia. Preferred expression vectors for use in yeast systems include, but are not limited to pYES2, pYD1, pTEF1/Zeo, pYES2/GS, pPICZ,pGAPZ, pGAPZalph, pPIC9, pPIC3.5, pHIL-D2, pHIL-S1, pPIC3.5K, pPIC9K, and PAO815 (all available from Invitrogen, Carlbad, CA). Other suitable vectors will be readily apparent to the skilled artisan.

Introduction of the construct into the host cell can be effected by calcium phosphate transfection, DEAE-dextran mediated transfection, cationic lipid-mediated transfection, electroporation, transduction, infection, or other methods. Such methods are described in many standard laboratory manuals, such as Davis et al., Basic Methods In Molecular Biology (1986). It is specifically contemplated that the polypeptides of the present invention may in fact be expressed by a host cell lacking a recombinant vector.

A polypeptide of this invention can be recovered and purified from recombinant cell cultures by well-known methods including ammonium sulfate or ethanol precipitation, acid extraction, anion or cation exchange chromatography, phosphocellulose chromatography, hydrophobic interaction chromatography, affinity chromatography, hydroxylapatite chromatography and lectin chromatography. Most preferably, high performance liquid chromatography ("HPLC") is employed for purification.

Polypeptides of the present invention, and preferably the secreted form, can also be recovered from: products purified from natural sources, including bodily fluids, tissues and cells, whether directly isolated or cultured; products of chemical synthetic procedures; and products produced by recombinant techniques from a prokaryotic or eukaryotic host, including, for example, bacterial, yeast, higher plant, insect, and mammalian cells. Depending upon the host employed in a recombinant production procedure, the polypeptides of the present invention may be glycosylated or may be non-glycosylated. In addition, polypeptides of the invention may also include an initial modified methionine residue, in some cases as a result of host-mediated processes. Thus, it is well known in the art that the N-terminal methionine encoded by the translation initiation codon generally is removed with high efficiency from any protein after translation in all eukaryotic cells. While the N-terminal methionine on most proteins also is efficiently removed in most prokaryotes, for some proteins, this prokaryotic removal process is inefficient, depending on the nature of the amino acid to which the N-terminal methionine is covalently linked.

In one embodiment, the yeast *Pichia pastoris* is used to express the polypeptide of the present invention in a eukaryotic system. *Pichia pastoris* is a methylotrophic yeast which can metabolize methanol as its sole carbon source. A

main step in the methanol metabolization pathway is the oxidation of methanol to formaldehyde using O_2. This reaction is catalyzed by the enzyme alcohol oxidase. In order to metabolize methanol as its sole carbon source, *Pichia pastoris* must generate high levels of alcohol oxidase due, in part, to the relatively low affinity of alcohol oxidase for O_2. Consequently, in a growth medium depending on methanol as a main carbon source, the promoter region of one of the two alcohol oxidase genes (*AOX1*) is highly active. In the presence of methanol, alcohol oxidase produced from the *AOX1* gene comprises up to approximately 30% of the total soluble protein in *Pichia pastoris*. *See*, Ellis, S.B., *et al., Mol. Cell. Biol.* 5:1111-21 (1985); Koutz, P.J, *et al., Yeast* 5:167-77 (1989); Tschopp, J.F., *et al., Nucl. Acids Res.* 15:3859-76 (1987). Thus, a heterologous coding sequence, such as, for example, a polynucleotide of the present invention, under the transcriptional regulation of all or part of the *AOX1* regulatory sequence is expressed at exceptionally high levels in *Pichia* yeast grown in the presence of methanol.

In one example, the plasmid vector pPIC9K is used to express DNA encoding a polypeptide of the invention, as set forth herein, in a *Pichea* yeast system essentially as described in "*Pichia* Protocols: Methods in Molecular Biology," D.R. Higgins and J. Cregg, eds. The Humana Press, Totowa, NJ, 1998. This expression vector allows expression and secretion of a protein of the invention by virtue of the strong *AOX1* promoter linked to the *Pichia pastoris* alkaline phosphatase (PHO) secretory signal peptide (i.e., leader) located upstream of a multiple cloning site.

Many other yeast vectors could be used in place of pPIC9K, such as, pYES2, pYD1, pTEF1/Zeo, pYES2/GS, pPICZ, pGAPZ, pGAPZalpha, pPIC9, pPIC3.5, pHIL-D2, pHIL-S1, pPIC3.5K, and PAO815, as one skilled in the art would readily appreciate, as long as the proposed expression construct provides appropriately located signals for transcription, translation, secretion (if desired), and the like, including an in-frame AUG as required.

In another embodiment, high-level expression of a heterologous coding sequence, such as, for example, a polynucleotide of the present invention, may be achieved by cloning the heterologous polynucleotide of the invention into an

expression vector such as, for example, pGAPZ or pGAPZalpha, and growing the yeast culture in the absence of methanol.

In addition to encompassing host cells containing the vector constructs discussed herein, the invention also encompasses primary, secondary, and immortalized host cells of vertebrate origin, particularly mammalian origin, that have been engineered to delete or replace endogenous genetic material (e.g., coding sequence), and/or to include genetic material (e.g., heterologous polynucleotide sequences) that is operably associated with the polynucleotides of the invention, and which activates, alters, and/or amplifies endogenous polynucleotides. For example, techniques known in the art may be used to operably associate heterologous control regions (e.g., promoter and/or enhancer) and endogenous polynucleotide sequences via homologous recombination, resulting in the formation of a new transcription unit (see, e.g., U.S. Patent No. 5,641,670, issued June 24, 1997; U.S. Patent No. 5,733,761, issued March 31, 1998; International Publication No. WO 96/29411, published September 26, 1996; International Publication No. WO 94/12650, published August 4, 1994; Koller et al., Proc. Natl. Acad. Sci. USA 86:8932-8935 (1989); and Zijlstra et al., Nature 342:435-438 (1989), the disclosures of each of which are incorporated by reference in their entireties).

In addition, polypeptides of the invention can be chemically synthesized using techniques known in the art (e.g., see Creighton, 1983, Proteins: Structures and Molecular Principles, W.H. Freeman & Co., N.Y., and Hunkapiller et al., *Nature*, 310:105-111 (1984)). For example, a polypeptide corresponding to a fragment of a polypeptide sequence of the invention can be synthesized by use of a peptide synthesizer. Furthermore, if desired, nonclassical amino acids or chemical amino acid analogs can be introduced as a substitution or addition into the polypeptide sequence. Non-classical amino acids include, but are not limited to, to the D-isomers of the common amino acids, 2,4-diaminobutyric acid, a-amino isobutyric acid, 4-aminobutyric acid, Abu, 2-amino butyric acid, g-Abu, e-Ahx, 6-amino hexanoic acid, Aib, 2-amino isobutyric acid, 3-amino propionic acid, ornithine, norleucine, norvaline, hydroxyproline, sarcosine, citrulline, homocitrulline, cysteic acid, t-butylglycine, t-butylalanine, phenylglycine, cyclohexylalanine, b-alanine, fluoro-amino acids, designer amino acids such as b-methyl amino acids, Ca-methyl amino

acids, Na-methyl amino acids, and amino acid analogs in general. Furthermore, the amino acid can be D (dextrorotary) or L (levorotary).

The invention encompasses polypeptides which are differentially modified during or after translation, *e.g.*, by glycosylation, acetylation, phosphorylation, amidation, derivatization by known protecting/blocking groups, proteolytic cleavage, linkage to an antibody molecule or other cellular ligand, etc. Any of numerous chemical modifications may be carried out by known techniques, including but not limited, to specific chemical cleavage by cyanogen bromide, trypsin, chymotrypsin, papain, V8 protease, $NaBH_4$; acetylation, formylation, oxidation, reduction; metabolic synthesis in the presence of tunicamycin; etc.

Additional post-translational modifications encompassed by the invention include, for example, e.g., N-linked or O-linked carbohydrate chains, processing of N-terminal or C-terminal ends), attachment of chemical moieties to the amino acid backbone, chemical modifications of N-linked or O-linked carbohydrate chains, and addition or deletion of an N-terminal methionine residue as a result of procaryotic host cell expression. The polypeptides may also be modified with a detectable label, such as an enzymatic, fluorescent, isotopic or affinity label to allow for detection and isolation of the protein.

Also provided by the invention are chemically modified derivatives of the polypeptides of the invention which may provide additional advantages such as increased solubility, stability and circulating time of the polypeptide, or decreased immunogenicity (see U.S. Patent NO: 4,179,337). The chemical moieties for derivitization may be selected from water soluble polymers such as polyethylene glycol, ethylene glycol/propylene glycol copolymers, carboxymethylcellulose, dextran, polyvinyl alcohol and the like. The polypeptides may be modified at random positions within the molecule, or at predetermined positions within the molecule and may include one, two, three or more attached chemical moieties.

The polymer may be of any molecular weight, and may be branched or unbranched. For polyethylene glycol, the preferred molecular weight is between about l kDa and about 100 kDa (the term "about" indicating that in preparations of polyethylene glycol, some molecules will weigh more, some less, than the stated molecular weight) for ease in handling and manufacturing. Other sizes may be used,

depending on the desired therapeutic profile (e.g., the duration of sustained release desired, the effects, if any on biological activity, the ease in handling, the degree or lack of antigenicity and other known effects of the polyethylene glycol to a therapeutic protein or analog). For example, the polyethylene glycol may have an average molecular weight of about 200, 500, 1000, 1500, 2000, 2500, 3000, 3500, 4000, 4500, 5000, 5500, 6000, 6500, 7000, 7500, 8000, 8500, 9000, 9500, 10,000, 10,500, 11,000, 11,500, 12,000, 12,500, 13,000, 13,500, 14,000, 14,500, 15,000, 15,500, 16,000, 16,500, 17,000, 17,500, 18,000, 18,500, 19,000, 19,500, 20,000, 25,000, 30,000, 35,000, 40,000, 50,000, 55,000, 60,000, 65,000, 70,000, 75,000, 80,000, 85,000, 90,000, 95,000, or 100,000 kDa.

As noted above, the polyethylene glycol may have a branched structure. Branched polyethylene glycols are described, for example, in U.S. Patent No. 5,643,575; Morpurgo *et al., Appl. Biochem. Biotechnol. 56*:59-72 (1996); Vorobjev *et al., Nucleosides Nucleotides 18*:2745-2750 (1999); and Caliceti *et al., Bioconjug. Chem. 10*:638-646 (1999), the disclosures of each of which are incorporated herein by reference.

The polyethylene glycol molecules (or other chemical moieties) should be attached to the protein with consideration of effects on functional or antigenic domains of the protein. There are a number of attachment methods available to those skilled in the art, e.g., EP 0 401 384, herein incorporated by reference (coupling PEG to G-CSF), see also Malik et al., Exp. Hematol. 20:1028-1035 (1992) (reporting pegylation of GM-CSF using tresyl chloride). For example, polyethylene glycol may be covalently bound through amino acid residues via a reactive group, such as, a free amino or carboxyl group. Reactive groups are those to which an activated polyethylene glycol molecule may be bound. The amino acid residues having a free amino group may include lysine residues and the N-terminal amino acid residues; those having a free carboxyl group may include aspartic acid residues glutamic acid residues and the C-terminal amino acid residue. Sulfhydryl groups may also be used as a reactive group for attaching the polyethylene glycol molecules. Preferred for therapeutic purposes is attachment at an amino group, such as attachment at the N-terminus or lysine group.

As suggested above, polyethylene glycol may be attached to proteins via linkage to any of a number of amino acid residues. For example, polyethylene glycol can be linked to a proteins via covalent bonds to lysine, histidine, aspartic acid, glutamic acid, or cysteine residues. One or more reaction chemistries may be employed to attach polyethylene glycol to specific amino acid residues (e.g., lysine, histidine, aspartic acid, glutamic acid, or cysteine) of the protein or to more than one type of amino acid residue (e.g., lysine, histidine, aspartic acid, glutamic acid, cysteine and combinations thereof) of the protein.

One may specifically desire proteins chemically modified at the N-terminus. Using polyethylene glycol as an illustration of the present composition, one may select from a variety of polyethylene glycol molecules (by molecular weight, branching, etc.), the proportion of polyethylene glycol molecules to protein (polypeptide) molecules in the reaction mix, the type of pegylation reaction to be performed, and the method of obtaining the selected N-terminally pegylated protein. The method of obtaining the N-terminally pegylated preparation (i.e., separating this moiety from other monopegylated moieties if necessary) may be by purification of the N-terminally pegylated material from a population of pegylated protein molecules. Selective proteins chemically modified at the N-terminus modification may be accomplished by reductive alkylation which exploits differential reactivity of different types of primary amino groups (lysine versus the N-terminal) available for derivatization in a particular protein. Under the appropriate reaction conditions, substantially selective derivatization of the protein at the N-terminus with a carbonyl group containing polymer is achieved.

As indicated above, pegylation of the proteins of the invention may be accomplished by any number of means. For example, polyethylene glycol may be attached to the protein either directly or by an intervening linker. Linkerless systems for attaching polyethylene glycol to proteins are described in Delgado *et al., Crit. Rev. Thera. Drug Carrier Sys. 9*:249-304 (1992); Francis *et al., Intern. J. of Hematol. 68*:1-18 (1998); U.S. Patent No. 4,002,531; U.S. Patent No. 5,349,052; WO 95/06058; and WO 98/32466, the disclosures of each of which are incorporated herein by reference.

One system for attaching polyethylene glycol directly to amino acid residues of proteins without an intervening linker employs tresylated MPEG, which is produced by the modification of monmethoxy polyethylene glycol (MPEG) using tresylchloride ($ClSO_2CH_2CF_3$). Upon reaction of protein with tresylated MPEG, polyethylene glycol is directly attached to amine groups of the protein. Thus, the invention includes protein-polyethylene glycol conjugates produced by reacting proteins of the invention with a polyethylene glycol molecule having a 2,2,2-trifluoreothane sulphonyl group.

Polyethylene glycol can also be attached to proteins using a number of different intervening linkers. For example, U.S. Patent No. 5,612,460, the entire disclosure of which is incorporated herein by reference, discloses urethane linkers for connecting polyethylene glycol to proteins. Protein-polyethylene glycol conjugates wherein the polyethylene glycol is attached to the protein by a linker can also be produced by reaction of proteins with compounds such as MPEG-succinimidylsuccinate, MPEG activated with 1,1'-carbonyldiimidazole, MPEG-2,4,5-trichloropenylcarbonate, MPEG-p-nitrophenolcarbonate, and various MPEG-succinate derivatives. A number additional polyethylene glycol derivatives and reaction chemistries for attaching polyethylene glycol to proteins are described in WO 98/32466, the entire disclosure of which is incorporated herein by reference. Pegylated protein products produced using the reaction chemistries set out herein are included within the scope of the invention.

The number of polyethylene glycol moieties attached to each protein of the invention (*i.e.*, the degree of substitution) may also vary. For example, the pegylated proteins of the invention may be linked, on average, to 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 15, 17, 20, or more polyethylene glycol molecules. Similarly, the average degree of substitution within ranges such as 1-3, 2-4, 3-5, 4-6, 5-7, 6-8, 7-9, 8-10, 9-11, 10-12, 11-13, 12-14, 13-15, 14-16, 15-17, 16-18, 17-19, or 18-20 polyethylene glycol moieties per protein molecule. Methods for determining the degree of substitution are discussed, for example, in Delgado *et al., Crit. Rev. Thera. Drug Carrier Sys. 9*:249-304 (1992).

The polypeptides of the invention may be in monomers or multimers (i.e., dimers, trimers, tetramers and higher multimers). Accordingly, the present invention

relates to monomers and multimers of the polypeptides of the invention, their preparation, and compositions (preferably, *Therapeutics*) containing them. In specific embodiments, the polypeptides of the invention are monomers, dimers, trimers or tetramers. In additional embodiments, the multimers of the invention are at least dimers, at least trimers, or at least tetramers.

Multimers encompassed by the invention may be homomers or heteromers. As used herein, the term homomer, refers to a multimer containing only polypeptides corresponding to the amino acid sequence of SEQ ID NO:Y or encoded by the cDNA contained in a deposited clone (including fragments, variants, splice variants, and fusion proteins, corresponding to these polypeptides as described herein). These homomers may contain polypeptides having identical or different amino acid sequences. In a specific embodiment, a homomer of the invention is a multimer containing only polypeptides having an identical amino acid sequence. In another specific embodiment, a homomer of the invention is a multimer containing polypeptides having different amino acid sequences. In specific embodiments, the multimer of the invention is a homodimer (*e.g.*, containing polypeptides having identical or different amino acid sequences) or a homotrimer (*e.g.*, containing polypeptides having identical and/or different amino acid sequences). In additional embodiments, the homomeric multimer of the invention is at least a homodimer, at least a homotrimer, or at least a homotetramer.

As used herein, the term heteromer refers to a multimer containing one or more heterologous polypeptides (*i.e.*, polypeptides of different proteins) in addition to the polypeptides of the invention. In a specific embodiment, the multimer of the invention is a heterodimer, a heterotrimer, or a heterotetramer. In additional embodiments, the heteromeric multimer of the invention is at least a heterodimer, at least a heterotrimer, or at least a heterotetramer.

Multimers of the invention may be the result of hydrophobic, hydrophilic, ionic and/or covalent associations and/or may be indirectly linked, by for example, liposome formation. Thus, in one embodiment, multimers of the invention, such as, for example, homodimers or homotrimers, are formed when polypeptides of the invention contact one another in solution. In another embodiment, heteromultimers of the invention, such as, for example, heterotrimers or heterotetramers, are formed

when polypeptides of the invention contact antibodies to the polypeptides of the invention (including antibodies to the heterologous polypeptide sequence in a fusion protein of the invention) in solution. In other embodiments, multimers of the invention are formed by covalent associations with and/or between the polypeptides of the invention. Such covalent associations may involve one or more amino acid residues contained in the polypeptide sequence (e.g., that recited in the sequence listing, or contained in the polypeptide encoded by a deposited clone). In one instance, the covalent associations are cross-linking between cysteine residues located within the polypeptide sequences which interact in the native (i.e., naturally occurring) polypeptide. In another instance, the covalent associations are the consequence of chemical or recombinant manipulation. Alternatively, such covalent associations may involve one or more amino acid residues contained in the heterologous polypeptide sequence in a fusion protein of the invention.

In one example, covalent associations are between the heterologous sequence contained in a fusion protein of the invention (see, e.g., US Patent Number 5,478,925). In a specific example, the covalent associations are between the heterologous sequence contained in an Fc fusion protein of the invention (as described herein). In another specific example, covalent associations of fusion proteins of the invention are between heterologous polypeptide sequence from another protein that is capable of forming covalently associated multimers, such as for example, oseteoprotegerin (see, e.g., International Publication NO: WO 98/49305, the contents of which are herein incorporated by reference in its entirety). In another embodiment, two or more polypeptides of the invention are joined through peptide linkers. Examples include those peptide linkers described in U.S. Pat. No. 5,073,627 (hereby incorporated by reference). Proteins comprising multiple polypeptides of the invention separated by peptide linkers may be produced using conventional recombinant DNA technology.

Another method for preparing multimer polypeptides of the invention involves use of polypeptides of the invention fused to a leucine zipper or isoleucine zipper polypeptide sequence. Leucine zipper and isoleucine zipper domains are polypeptides that promote multimerization of the proteins in which they are found. Leucine zippers were originally identified in several DNA-binding proteins (Landschulz et al.,

Science 240:1759, (1988)), and have since been found in a variety of different proteins. Among the known leucine zippers are naturally occurring peptides and derivatives thereof that dimerize or trimerize. Examples of leucine zipper domains suitable for producing soluble multimeric proteins of the invention are those described in PCT application WO 94/10308, hereby incorporated by reference. Recombinant fusion proteins comprising a polypeptide of the invention fused to a polypeptide sequence that dimerizes or trimerizes in solution are expressed in suitable host cells, and the resulting soluble multimeric fusion protein is recovered from the culture supernatant using techniques known in the art.

Trimeric polypeptides of the invention may offer the advantage of enhanced biological activity. Preferred leucine zipper moieties and isoleucine moieties are those that preferentially form trimers. One example is a leucine zipper derived from lung surfactant protein D (SPD), as described in Hoppe et al. (FEBS Letters 344:191, (1994)) and in U.S. patent application Ser. No. 08/446,922, hereby incorporated by reference. Other peptides derived from naturally occurring trimeric proteins may be employed in preparing trimeric polypeptides of the invention.

In another example, proteins of the invention are associated by interactions between Flag® polypeptide sequence contained in fusion proteins of the invention containing Flag® polypeptide seuqence. In a further embodiment, associations proteins of the invention are associated by interactions between heterologous polypeptide sequence contained in Flag® fusion proteins of the invention and anti-Flag® antibody.

The multimers of the invention may be generated using chemical techniques known in the art. For example, polypeptides desired to be contained in the multimers of the invention may be chemically cross-linked using linker molecules and linker molecule length optimization techniques known in the art (see, e.g., US Patent Number 5,478,925, which is herein incorporated by reference in its entirety). Additionally, multimers of the invention may be generated using techniques known in the art to form one or more inter-molecule cross-links between the cysteine residues located within the sequence of the polypeptides desired to be contained in the multimer (see, e.g., US Patent Number 5,478,925, which is herein incorporated by reference in its entirety). Further, polypeptides of the invention may be routinely

modified by the addition of cysteine or biotin to the C terminus or N-terminus of the polypeptide and techniques known in the art may be applied to generate multimers containing one or more of these modified polypeptides (see, e.g., US Patent Number 5,478,925, which is herein incorporated by reference in its entirety). Additionally, techniques known in the art may be applied to generate liposomes containing the polypeptide components desired to be contained in the multimer of the invention (see, e.g., US Patent Number 5,478,925, which is herein incorporated by reference in its entirety).

Alternatively, multimers of the invention may be generated using genetic engineering techniques known in the art. In one embodiment, polypeptides contained in multimers of the invention are produced recombinantly using fusion protein technology described herein or otherwise known in the art (see, e.g., US Patent Number 5,478,925, which is herein incorporated by reference in its entirety). In a specific embodiment, polynucleotides coding for a homodimer of the invention are generated by ligating a polynucleotide sequence encoding a polypeptide of the invention to a sequence encoding a linker polypeptide and then further to a synthetic polynucleotide encoding the translated product of the polypeptide in the reverse orientation from the original C-terminus to the N-terminus (lacking the leader sequence) (see, e.g., US Patent Number 5,478,925, which is herein incorporated by reference in its entirety). In another embodiment, recombinant techniques described herein or otherwise known in the art are applied to generate recombinant polypeptides of the invention which contain a transmembrane domain (or hyrophobic or signal peptide) and which can be incorporated by membrane reconstitution techniques into liposomes (see, e.g., US Patent Number 5,478,925, which is herein incorporated by reference in its entirety).

Uses of the Polynucleotides

Each of the polynucleotides identified herein can be used in numerous ways as reagents. The following description should be considered exemplary and utilizes known techniques.

The polynucleotides of the present invention are useful for chromosome identification. There exists an ongoing need to identify new chromosome markers,

since few chromosome marking reagents, based on actual sequence data (repeat polymorphisms), are presently available. Each polynucleotide of the present invention can be used as a chromosome marker.

Briefly, sequences can be mapped to chromosomes by preparing PCR primers (preferably 15-25 bp) from the sequences shown in SEQ ID NO:X. Primers can be selected using computer analysis so that primers do not span more than one predicted exon in the genomic DNA. These primers are then used for PCR screening of somatic cell hybrids containing individual human chromosomes. Only those hybrids containing the human gene corresponding to the SEQ ID NO:X will yield an amplified fragment.

Similarly, somatic hybrids provide a rapid method of PCR mapping the polynucleotides to particular chromosomes. Three or more clones can be assigned per day using a single thermal cycler. Moreover, sublocalization of the polynucleotides can be achieved with panels of specific chromosome fragments. Other gene mapping strategies that can be used include in situ hybridization, prescreening with labeled flow-sorted chromosomes, preselection by hybridization to construct chromosome specific-cDNA libraries and computer mapping techniques (See, e.g., Shuler, Trends Biotechnol 16:456-459 (1998) which is hereby incorporated by reference in its entirety)..

Precise chromosomal location of the polynucleotides can also be achieved using fluorescence in situ hybridization (FISH) of a metaphase chromosomal spread. This technique uses polynucleotides as short as 500 or 600 bases; however, polynucleotides 2,000-4,000 bp are preferred. For a review of this technique, see Verma et al., "Human Chromosomes: a Manual of Basic Techniques," Pergamon Press, New York (1988).

For chromosome mapping, the polynucleotides can be used individually (to mark a single chromosome or a single site on that chromosome) or in panels (for marking multiple sites and/or multiple chromosomes).

The polynucleotides of the present invention would likewise be useful for radiation hybrid mapping, HAPPY mapping, and long range restriction mapping. For a review of these techniques and others known in the art, see, e.g., Dear, "Genome Mapping: A Practical Approach," IRL Press at Oxford University Press, London

(1997); Aydin, J. Mol. Med. 77:691-694 (1999); Hacia et al., Mol. Psychiatry 3:483-492 (1998); Herrick et al., Chromosome Res. 7:409-423 (1999); Hamilton et al., Methods Cell Biol. 62:265-280 (2000); and/or Ott, J. Hered. 90:68-70 (1999) each of which is hereby incorporated by reference in its entirety.

Once a polynucleotide has been mapped to a precise chromosomal location, the physical position of the polynucleotide can be used in linkage analysis. Linkage analysis establishes coinheritance between a chromosomal location and presentation of a particular disease. (Disease mapping data are found, for example, in V. McKusick, Mendelian Inheritance in Man (available on line through Johns Hopkins University Welch Medical Library) .) Assuming 1 megabase mapping resolution and one gene per 20 kb, a cDNA precisely localized to a chromosomal region associated with the disease could be one of 50-500 potential causative genes.

Thus, once coinheritance is established, differences in the polynucleotide and the corresponding gene between affected and unaffected individuals can be examined. First, visible structural alterations in the chromosomes, such as deletions or translocations, are examined in chromosome spreads or by PCR. If no structural alterations exist, the presence of point mutations are ascertained. Mutations observed in some or all affected individuals, but not in normal individuals, indicates that the mutation may cause the disease. However, complete sequencing of the polypeptide and the corresponding gene from several normal individuals is required to distinguish the mutation from a polymorphism. If a new polymorphism is identified, this polymorphic polypeptide can be used for further linkage analysis.

Furthermore, increased or decreased expression of the gene in affected individuals as compared to unaffected individuals can be assessed using polynucleotides of the present invention. Any of these alterations (altered expression, chromosomal rearrangement, or mutation) can be used as a diagnostic or prognostic marker.

Thus, the invention also provides a diagnostic method useful during diagnosis of a disorder, involving measuring the expression level of polynucleotides of the present invention in cells or body fluid from an individual and comparing the measured gene expression level with a standard level of polynucleotide expression

level, whereby an increase or decrease in the gene expression level compared to the standard is indicative of a disorder.

In still another embodiment, the invention includes a kit for analyzing samples for the presence of proliferative and/or cancerous polynucleotides derived from a test subject. In a general embodiment, the kit includes at least one polynucleotide probe containing a nucleotide sequence that will specifically hybridize with a polynucleotide of the present invention and a suitable container. In a specific embodiment, the kit includes two polynucleotide probes defining an internal region of the polynucleotide of the present invention, where each probe has one strand containing a 31'mer-end internal to the region. In a further embodiment, the probes may be useful as primers for polymerase chain reaction amplification.

Where a diagnosis of a disorder, has already been made according to conventional methods, the present invention is useful as a prognostic indicator, whereby patients exhibiting enhanced or depressed polynucleotide of the present invention expression will experience a worse clinical outcome relative to patients expressing the gene at a level nearer the standard level.

By "measuring the expression level of polynucleotide of the present invention" is intended qualitatively or quantitatively measuring or estimating the level of the polypeptide of the present invention or the level of the mRNA encoding the polypeptide in a first biological sample either directly (e.g., by determining or estimating absolute protein level or mRNA level) or relatively (e.g., by comparing to the polypeptide level or mRNA level in a second biological sample). Preferably, the polypeptide level or mRNA level in the first biological sample is measured or estimated and compared to a standard polypeptide level or mRNA level, the standard being taken from a second biological sample obtained from an individual not having the disorder or being determined by averaging levels from a population of individuals not having a disorder. As will be appreciated in the art, once a standard polypeptide level or mRNA level is known, it can be used repeatedly as a standard for comparison.

By "biological sample" is intended any biological sample obtained from an individual, body fluid, cell line, tissue culture, or other source which contains the polypeptide of the present invention or mRNA. As indicated, biological samples

include body fluids (such as semen, lymph, sera, plasma, urine, synovial fluid and spinal fluid) which contain the polypeptide of the present invention, and other tissue sources found to express the polypeptide of the present invention. Methods for obtaining tissue biopsies and body fluids from mammals are well known in the art. Where the biological sample is to include mRNA, a tissue biopsy is the preferred source.

The method(s) provided above may preferrably be applied in a diagnostic method and/or kits in which polynucleotides and/or polypeptides are attached to a solid support. In one exemplary method, the support may be a "gene chip" or a "biological chip" as described in US Patents 5,837,832, 5,874,219, and 5,856,174. Further, such a gene chip with polynucleotides of the present invention attached may be used to identify polymorphisms between the polynucleotide sequences, with polynucleotides isolated from a test subject. The knowledge of such polymorphisms (i.e. their location, as well as, their existence) would be beneficial in identifying disease loci for many disorders, including cancerous diseases and conditions. Such a method is described in US Patents 5,858,659 and 5,856,104. The US Patents referenced supra are hereby incorporated by reference in their entirety herein.

The present invention encompasses polynucleotides of the present invention that are chemically synthesized, or reproduced as peptide nucleic acids (PNA), or according to other methods known in the art. The use of PNAs would serve as the preferred form if the polynucleotides are incorporated onto a solid support, or gene chip. For the purposes of the present invention, a peptide nucleic acid (PNA) is a polyamide type of DNA analog and the monomeric units for adenine, guanine, thymine and cytosine are available commercially (Perceptive Biosystems). Certain components of DNA, such as phosphorus, phosphorus oxides, or deoxyribose derivatives, are not present in PNAs. As disclosed by P. E. Nielsen, M. Egholm, R. H. Berg and O. Buchardt, Science 254, 1497 (1991); and M. Egholm, O. Buchardt, L.Christensen, C. Behrens, S. M. Freier, D. A. Driver, R. H. Berg, S. K. Kim, B. Norden, and P. E. Nielsen, Nature 365, 666 (1993), PNAs bind specifically and tightly to complementary DNA strands and are not degraded by nucleases. In fact, PNA binds more strongly to DNA than DNA itself does. This is probably because there is no electrostatic repulsion between the two strands, and also the polyamide

backbone is more flexible. Because of this, PNA/DNA duplexes bind under a wider range of stringency conditions than DNA/DNA duplexes, making it easier to perform multiplex hybridization. Smaller probes can be used than with DNA due to the strong binding. In addition, it is more likely that single base mismatches can be determined with PNA/DNA hybridization because a single mismatch in a PNA/DNA 15-mer lowers the melting point (T.sub.m) by 8°-20° C, vs. 4°-16° C for the DNA/DNA 15-mer duplex. Also, the absence of charge groups in PNA means that hybridization can be done at low ionic strengths and reduce possible interference by salt during the analysis.

The present invention is useful for detecting cancer in mammals. In particular the invention is useful during diagnosis of pathological cell proliferative neoplasias which include, but are not limited to: acute myelogenous leukemias including acute monocytic leukemia, acute myeloblastic leukemia, acute promyelocytic leukemia, acute myelomonocytic leukemia, acute erythroleukemia, acute megakaryocytic leukemia, and acute undifferentiated leukemia, etc.; and chronic myelogenous leukemias including chronic myelomonocytic leukemia, chronic granulocytic leukemia, etc. Preferred mammals include monkeys, apes, cats, dogs, cows, pigs, horses, rabbits and humans. Particularly preferred are humans.

Pathological cell proliferative diseases, disorders, and/or conditions are often associated with inappropriate activation of proto-oncogenes. (Gelmann, E. P. et al., "The Etiology of Acute Leukemia: Molecular Genetics and Viral Oncology," in Neoplastic Diseases of the Blood, Vol 1., Wiemik, P. H. et al. eds., 161-182 (1985)). Neoplasias are now believed to result from the qualitative alteration of a normal cellular gene product, or from the quantitative modification of gene expression by insertion into the chromosome of a viral sequence, by chromosomal translocation of a gene to a more actively transcribed region, or by some other mechanism. (Gelmann et al., supra) It is likely that mutated or altered expression of specific genes is involved in the pathogenesis of some leukemias, among other tissues and cell types. (Gelmann et al., supra) Indeed, the human counterparts of the oncogenes involved in some animal neoplasias have been amplified or translocated in some cases of human leukemia and carcinoma. (Gelmann et al., supra)

For example, c-myc expression is highly amplified in the non-lymphocytic leukemia cell line HL-60. When HL-60 cells are chemically induced to stop proliferation, the level of c-myc is found to be downregulated. (International Publication Number WO 91/15580) However, it has been shown that exposure of HL-60 cells to a DNA construct that is complementary to the 5' end of c-myc or c-myb blocks translation of the corresponding mRNAs which downregulates expression of the c-myc or c-myb proteins and causes arrest of cell proliferation and differentiation of the treated cells. (International Publication Number WO 91/15580; Wickstrom et al., Proc. Natl. Acad. Sci. 85:1028 (1988); Anfossi et al., Proc. Natl. Acad. Sci. 86:3379 (1989)). However, the skilled artisan would appreciate the present invention's usefulness would not be limited to treatment of proliferative diseases, disorders, and/or conditions of hematopoietic cells and tissues, in light of the numerous cells and cell types of varying origins which are known to exhibit proliferative phenotypes.

In addition to the foregoing, a polynucleotide can be used to control gene expression through triple helix formation or antisense DNA or RNA. Antisense techniques are discussed, for example, in Okano, J. Neurochem. 56: 560 (1991); "Oligodeoxynucleotides as Antisense Inhibitors of Gene Expression,CRCPress, Boca Raton, FL (1988). Triple helix formation is discussed in, for instance Lee et al., Nucleic Acids Research 6: 3073 (1979); Cooney et al., Science 241: 456 (1988); and Dervan et al., Science 251: 1360 (1991). Both methods rely on binding of the polynucleotide to a complementary DNA or RNA. For these techniques, preferred polynucleotides are usually oligonucleotides 20 to 40 bases in length and complementary to either the region of the gene involved in transcription (triple helix - see Lee et al., Nucl. Acids Res. 6:3073 (1979); Cooney et al., Science 241:456 (1988); and Dervan et al., Science 251:1360 (1991)) or to the mRNA itself (antisense - Okano, J. Neurochem. 56:560 (1991); Oligodeoxy-nucleotides as Antisense Inhibitors of Gene Expression, CRC Press, Boca Raton, FL (1988).) Triple helix formation optimally results in a shut-off of RNA transcription from DNA, while antisense RNA hybridization blocks translation of an mRNA molecule into polypeptide. Both techniques are effective in model systems, and the information

disclosed herein can be used to design antisense or triple helix polynucleotides in an effort to treat or prevent disease.

Polynucleotides of the present invention are also useful in gene therapy. One goal of gene therapy is to insert a normal gene into an organism having a defective gene, in an effort to correct the genetic defect. The polynucleotides disclosed in the present invention offer a means of targeting such genetic defects in a highly accurate manner. Another goal is to insert a new gene that was not present in the host genome, thereby producing a new trait in the host cell.

The polynucleotides are also useful for identifying individuals from minute biological samples. The United States military, for example, is considering the use of restriction fragment length polymorphism (RFLP) for identification of its personnel. In this technique, an individual's genomic DNA is digested with one or more restriction enzymes, and probed on a Southern blot to yield unique bands for identifying personnel. This method does not suffer from the current limitations of "Dog Tags" which can be lost, switched, or stolen, making positive identification difficult. The polynucleotides of the present invention can be used as additional DNA markers for RFLP.

The polynucleotides of the present invention can also be used as an alternative to RFLP, by determining the actual base-by-base DNA sequence of selected portions of an individual's genome. These sequences can be used to prepare PCR primers for amplifying and isolating such selected DNA, which can then be sequenced. Using this technique, individuals can be identified because each individual will have a unique set of DNA sequences. Once an unique ID database is established for an individual, positive identification of that individual, living or dead, can be made from extremely small tissue samples.

Forensic biology also benefits from using DNA-based identification techniques as disclosed herein. DNA sequences taken from very small biological samples such as tissues, e.g., hair or skin, or body fluids, e.g., blood, saliva, semen, synovial fluid, amniotic fluid, breast milk, lymph, pulmonary sputum or surfactant,urine,fecal matter, etc., can be amplified using PCR. In one prior art technique, gene sequences amplified from polymorphic loci, such as DQa class II HLA gene, are used in forensic biology to identify individuals. (Erlich, H., PCR

Technology, Freeman and Co. (1992).) Once these specific polymorphic loci are amplified, they are digested with one or more restriction enzymes, yielding an identifying set of bands on a Southern blot probed with DNA corresponding to the DQa class II HLA gene. Similarly, polynucleotides of the present invention can be used as polymorphic markers for forensic purposes.

There is also a need for reagents capable of identifying the source of a particular tissue. Such need arises, for example, in forensics when presented with tissue of unknown origin. Appropriate reagents can comprise, for example, DNA probes or primers specific to particular tissue prepared from the sequences of the present invention. Panels of such reagents can identify tissue by species and/or by organ type. In a similar fashion, these reagents can be used to screen tissue cultures for contamination.

In the very least, the polynucleotides of the present invention can be used as molecular weight markers on Southern gels, as diagnostic probes for the presence of a specific mRNA in a particular cell type, as a probe to "subtract-out" known sequences in the process of discovering novel polynucleotides, for selecting and making oligomers for attachment to a "gene chip" or other support, to raise anti-DNA antibodies using DNA immunization techniques, and as an antigen to elicit an immune response.

Uses of the Polypeptides

Each of the polypeptides identified herein can be used in numerous ways. The following description should be considered exemplary and utilizes known techniques.

A polypeptide of the present invention can be used to assay protein levels in a biological sample using antibody-based techniques. For example, protein expression in tissues can be studied with classical immunohistological methods. (Jalkanen, M., et al., J. Cell. Biol. 101:976-985 (1985); Jalkanen, M., et al., J. Cell . Biol. 105:3087-3096 (1987).) Other antibody-based methods useful for detecting protein gene expression include immunoassays, such as the enzyme linked immunosorbent assay (ELISA) and the radioimmunoassay (RIA). Suitable antibody assay labels are known in the art and include enzyme labels, such as, glucose oxidase, and radioisotopes, such as iodine (125I, 121I), carbon (14C), sulfur (35S), tritium (3H), indium (112In), and

technetium (99mTc), and fluorescent labels, such as fluorescein and rhodamine, and biotin.

In addition to assaying secreted protein levels in a biological sample, proteins can also be detected in vivo by imaging. Antibody labels or markers for in vivo imaging of protein include those detectable by X-radiography, NMR or ESR. For X-radiography, suitable labels include radioisotopes such as barium or cesium, which emit detectable radiation but are not overtly harmful to the subject. Suitable markers for NMR and ESR include those with a detectable characteristic spin, such as deuterium, which may be incorporated into the antibody by labeling of nutrients for the relevant hybridoma.

A protein-specific antibody or antibody fragment which has been labeled with an appropriate detectable imaging moiety, such as a radioisotope (for example, 131I, 112In, 99mTc), a radio-opaque substance, or a material detectable by nuclear magnetic resonance, is introduced (for example, parenterally, subcutaneously, or intraperitoneally) into the mammal. It will be understood in the art that the size of the subject and the imaging system used will determine the quantity of imaging moiety needed to produce diagnostic images. In the case of a radioisotope moiety, for a human subject, the quantity of radioactivity injected will normally range from about 5 to 20 millicuries of 99mTc. The labeled antibody or antibody fragment will then preferentially accumulate at the location of cells which contain the specific protein. In vivo tumor imaging is described in S.W. Burchiel et al., "Immunopharmacokinetics of Radiolabeled Antibodies and Their Fragments." (Chapter 13 in Tumor Imaging: The Radiochemical Detection of Cancer, S.W. Burchiel and B. A. Rhodes, eds., Masson Publishing Inc. (1982).)

Thus, the invention provides a diagnostic method of a disorder, which involves (a) assaying the expression of a polypeptide of the present invention in cells or body fluid of an individual; (b) comparing the level of gene expression with a standard gene expression level, whereby an increase or decrease in the assayed polypeptide gene expression level compared to the standard expression level is indicative of a disorder. With respect to cancer, the presence of a relatively high amount of transcript in biopsied tissue from an individual may indicate a predisposition for the development of the disease, or may provide a means for

detecting the disease prior to the appearance of actual clinical symptoms. A more definitive diagnosis of this type may allow health professionals to employ preventative measures or aggressive treatment earlier thereby preventing the development or further progression of the cancer.

Moreover, polypeptides of the present invention can be used to treat, prevent, and/or diagnose disease. For example, patients can be administered a polypeptide of the present invention in an effort to replace absent or decreased levels of the polypeptide (e.g., insulin), to supplement absent or decreased levels of a different polypeptide (e.g., hemoglobin S for hemoglobin B, SOD, catalase, DNA repair proteins), to inhibit the activity of a polypeptide (e.g., an oncogene or tumor supressor), to activate the activity of a polypeptide (e.g., by binding to a receptor), to reduce the activity of a membrane bound receptor by competing with it for free ligand (e.g., soluble TNF receptors used in reducing inflammation), or to bring about a desired response (e.g., blood vessel growth inhibition, enhancement of the immune response to proliferative cells or tissues).

Similarly, antibodies directed to a polypeptide of the present invention can also be used to treat, prevent, and/or diagnose disease. For example, administration of an antibody directed to a polypeptide of the present invention can bind and reduce overproduction of the polypeptide. Similarly, administration of an antibody can activate the polypeptide, such as by binding to a polypeptide bound to a membrane (receptor).

At the very least, the polypeptides of the present invention can be used as molecular weight markers on SDS-PAGE gels or on molecular sieve gel filtration columns using methods well known to those of skill in the art. Polypeptides can also be used to raise antibodies, which in turn are used to measure protein expression from a recombinant cell, as a way of assessing transformation of the host cell. Moreover, the polypeptides of the present invention can be used to test the following biological activities.

<u>Gene Therapy Methods</u>

Another aspect of the present invention is to gene therapy methods for treatingor preventing disorders, diseases and conditions. The gene therapy methods relate to the introduction of nucleic acid (DNA, RNA and antisense DNA or RNA) sequences into an animal to achieve expression of a polypeptide of the present invention. This method requires a polynucleotide which codes for a polypeptide of the invention that operatively linked to a promoter and any other genetic elements necessary for the expression of the polypeptide by the target tissue. Such gene therapy and delivery techniques are known in the art, see, for example, WO90/11092, which is herein incorporated by reference.

Thus, for example, cells from a patient may be engineered with a polynucleotide (DNA or RNA) comprising a promoter operably linked to a polynucleotide of the invention *ex vivo*, with the engineered cells then being provided to a patient to be treated with the polypeptide. Such methods are well-known in the art. For example, see Belldegrun et al., J. Natl. Cancer Inst., 85:207-216 (1993); Ferrantini et al., Cancer Research, 53:107-1112 (1993); Ferrantini et al., J. Immunology 153: 4604-4615 (1994); Kaido, T., et al., Int. J. Cancer 60: 221-229 (1995); Ogura et al., Cancer Research 50: 5102-5106 (1990); Santodonato, et al., Human Gene Therapy 7:1-10 (1996); Santodonato, et al., Gene Therapy 4:1246-1255 (1997); and Zhang, et al., Cancer Gene Therapy 3: 31-38 (1996)), which are herein incorporated by reference. In one embodiment, the cells which are engineered are arterial cells. The arterial cells may be reintroduced into the patient through direct injection to the artery, the tissues surrounding the artery, or through catheter injection.

As discussed in more detail below, the polynucleotide constructs can be delivered by any method that delivers injectable materials to the cells of an animal, such as, injection into the interstitial space of tissues (heart, muscle, skin, lung, liver, and the like). The polynucleotide constructs may be delivered in a pharmaceutically acceptable liquid or aqueous carrier.

In one embodiment, the polynucleotide of the invention is delivered as a naked polynucleotide. The term "naked" polynucleotide, DNA or RNA refers to sequences that are free from any delivery vehicle that acts to assist, promote or facilitate entry into the cell, including viral sequences, viral particles, liposome formulations,

lipofectin or precipitating agents and the like. However, the polynucleotides of the invention can also be delivered in liposome formulations and lipofectin formulations and the like can be prepared by methods well known to those skilled in the art. Such methods are described, for example, in U.S. Patent Nos. 5,593,972, 5,589,466, and 5,580,859, which are herein incorporated by reference.

The polynucleotide vector constructs of the invention used in the gene therapy method are preferably constructs that will not integrate into the host genome nor will they contain sequences that allow for replication. Appropriate vectors include pWLNEO, pSV2CAT, pOG44, pXT1 and pSG available from Stratagene; pSVK3, pBPV, pMSG and pSVL available from Pharmacia; and pEF1/V5, pcDNA3.1, and pRc/CMV2 available from Invitrogen. Other suitable vectors will be readily apparent to the skilled artisan.

Any strong promoter known to those skilled in the art can be used for driving the expression of polynucleotide sequence of the invention. Suitable promoters include adenoviral promoters, such as the adenoviral major late promoter; or heterologous promoters, such as the cytomegalovirus (CMV) promoter; the respiratory syncytial virus (RSV) promoter; inducible promoters, such as the MMT promoter, the metallothionein promoter; heat shock promoters; the albumin promoter; the ApoAI promoter; human globin promoters; viral thymidine kinase promoters, such as the Herpes Simplex thymidine kinase promoter; retroviral LTRs; the b-actin promoter; and human growth hormone promoters. The promoter also may be the native promoter for the polynucleotides of the invention.

Unlike other gene therapy techniques, one major advantage of introducing naked nucleic acid sequences into target cells is the transitory nature of the polynucleotide synthesis in the cells. Studies have shown that non-replicating DNA sequences can be introduced into cells to provide production of the desired polypeptide for periods of up to six months.

The polynucleotide construct of the invention can be delivered to the interstitial space of tissues within the an animal, including of muscle, skin, brain, lung, liver, spleen, bone marrow, thymus, heart, lymph, blood, bone, cartilage, pancreas, kidney, gall bladder, stomach, intestine, testis, ovary, uterus, rectum, nervous system, eye, gland, and connective tissue. Interstitial space of the tissues comprises the intercellular,

fluid, mucopolysaccharide matrix among the reticular fibers of organ tissues, elastic fibers in the walls of vessels or chambers, collagen fibers of fibrous tissues, or that same matrix within connective tissue ensheathing muscle cells or in the lacunae of bone. It is similarly the space occupied by the plasma of the circulation and the lymph fluid of the lymphatic channels. Delivery to the interstitial space of muscle tissue is preferred for the reasons discussed below. They may be conveniently delivered by injection into the tissues comprising these cells. They are preferably delivered to and expressed in persistent, non-dividing cells which are differentiated, although delivery and expression may be achieved in non-differentiated or less completely differentiated cells, such as, for example, stem cells of blood or skin fibroblasts. *In vivo* muscle cells are particularly competent in their ability to take up and express polynucleotides.

For the naked*nucleic* acid sequence injection, an effective dosage amount of DNA or RNA will be in the range of from about 0.05 mg/kg body weight to about 50 mg/kg body weight. Preferably the dosage will be from about 0.005 mg/kg to about 20 mg/kg and more preferably from about 0.05 mg/kg to about 5 mg/kg. Of course, as the artisan of ordinary skill will appreciate, this dosage will vary according to the tissue site of injection. The appropriate and effective dosage of nucleic acid sequence can readily be determined by those of ordinary skill in the art and may depend on the condition being treated and the route of administration.

The preferred route of administration is by the parenteral route of injection into the interstitial space of tissues. However, other parenteral routes may also be used, such as, inhalation of an aerosol formulation particularly for delivery to lungs or bronchial tissues, throat or mucous membranes of the nose. In addition, naked DNA constructs can be delivered to arteries during angioplasty by the catheter used in the procedure.

The naked polynucleotides are delivered by any method known in the art, including, but not limited to, direct needle injection at the delivery site, intravenous injection, topical administration, catheter infusion, and so-called "gene guns". These delivery methods are known in the art.

The constructs may also be delivered with delivery vehicles such as viral sequences, viral particles, liposome formulations, lipofectin, precipitating agents, etc. Such methods of delivery are known in the art.

In certain embodiments, the polynucleotide constructs of the invention are complexed in a liposome preparation. Liposomal preparations for use in the instant invention include cationic (positively charged), anionic (negatively charged) and neutral preparations. However, cationic liposomes are particularly preferred because a tight charge complex can be formed between the cationic liposome and the polyanionic nucleic acid. Cationic liposomes have been shown to mediate intracellular delivery of plasmid DNA (Felgner et al., Proc. Natl. Acad. Sci. USA , 84:7413-7416 (1987), which is herein incorporated by reference); mRNA (Malone et al., Proc. Natl. Acad. Sci. USA , 86:6077-6081 (1989), which is herein incorporated by reference); and purified transcription factors (Debs et al., J. Biol. Chem., 265:10189-10192 (1990), which is herein incorporated by reference), in functional form.

Cationic liposomes are readily available. For example, N[1-2,3-dioleyloxy)propyl]-N,N,N-triethylammonium (DOTMA) liposomes are particularly useful and are available under the trademark Lipofectin, from GIBCO BRL, Grand Island, N.Y. (See, also, Felgner et al., Proc. Natl Acad. Sci. USA , 84:7413-7416 (1987), which is herein incorporated by reference). Other commercially available liposomes include transfectace (DDAB/DOPE) and DOTAP/DOPE (Boehringer).

Other cationic liposomes can be prepared from readily available materials using techniques well known in the art. See, e.g. PCT Publication NO: WO 90/11092 (which is herein incorporated by reference) for a description of the synthesis of DOTAP (1,2-bis(oleoyloxy)-3-(trimethylammonio)propane) liposomes. Preparation of DOTMA liposomes is explained in the literature, see, e.g., Felgner et al., Proc. Natl. Acad. Sci. USA, 84:7413-7417, which is herein incorporated by reference. Similar methods can be used to prepare liposomes from other cationic lipid materials.

Similarly, anionic and neutral liposomes are readily available, such as from Avanti Polar Lipids (Birmingham, Ala.), or can be easily prepared using readily available materials. Such materials include phosphatidyl, choline, cholesterol, phosphatidyl ethanolamine, dioleoylphosphatidyl choline (DOPC), dioleoylphosphatidyl glycerol (DOPG), dioleoylphoshatidyl ethanolamine (DOPE), among others. These materials can also be mixed with the DOTMA and DOTAP

starting materials in appropriate ratios. Methods for making liposomes using these materials are well known in the art.

For example, commercially dioleoylphosphatidyl choline (DOPC), dioleoylphosphatidyl glycerol (DOPG), and dioleoylphosphatidyl ethanolamine (DOPE) can be used in various combinations to make conventional liposomes, with or without the addition of cholesterol. Thus, for example, DOPG/DOPC vesicles can be prepared by drying 50 mg each of DOPG and DOPC under a stream of nitrogen gas into a sonication vial. The sample is placed under a vacuum pump overnight and is hydrated the following day with deionized water. The sample is then sonicated for 2 hours in a capped vial, using a Heat Systems model 350 sonicator equipped with an inverted cup (bath type) probe at the maximum setting while the bath is circulated at 15EC. Alternatively, negatively charged vesicles can be prepared without sonication to produce multilamellar vesicles or by extrusion through nucleopore membranes to produce unilamellar vesicles of discrete size. Other methods are known and available to those of skill in the art.

The liposomes can comprise multilamellar vesicles (MLVs), small unilamellar vesicles (SUVs), or large unilamellar vesicles (LUVs), with SUVs being preferred. The various liposome-nucleic acid complexes are prepared using methods well known in the art. See, e.g., Straubinger et al., Methods of Immunology , 101:512-527 (1983), which is herein incorporated by reference. For example, MLVs containing nucleic acid can be prepared by depositing a thin film of phospholipid on the walls of a glass tube and subsequently hydrating with a solution of the material to be encapsulated. SUVs are prepared by extended sonication of MLVs to produce a homogeneous population of unilamellar liposomes. The material to be entrapped is added to a suspension of preformed MLVs and then sonicated. When using liposomes containing cationic lipids, the dried lipid film is resuspended in an appropriate solution such as sterile water or an isotonic buffer solution such as 10 mM Tris/NaCl, sonicated, and then the preformed liposomes are mixed directly with the DNA. The liposome and DNA form a very stable complex due to binding of the positively charged liposomes to the cationic DNA. SUVs find use with small nucleic acid fragments. LUVs are prepared by a number of methods, well known in the art. Commonly used methods include Ca^{2+}-EDTA chelation (Papahadjopoulos et al., Biochim. Biophys. Acta,

394:483 (1975); Wilson et al., Cell , 17:77 (1979)); ether injection (Deamer et al., Biochim. Biophys. Acta, 443:629 (1976); Ostro et al., Biochem. Biophys. Res. Commun., 76:836 (1977); Fraley et al., Proc. Natl. Acad. Sci. USA, 76:3348 (1979)); detergent dialysis (Enoch et al., Proc. Natl. Acad. Sci. USA , 76:145 (1979)); and reverse-phase evaporation (REV) (Fraley et al., J. Biol. Chem., 255:10431 (1980); Szoka et al., Proc. Natl. Acad. Sci. USA , 75:145 (1978); Schaefer-Ridder et al., Science, 215:166 (1982)), which are herein incorporated by reference.

Generally, the ratio of DNA to liposomes will be from about 10:1 to about 1:10. Preferably, the ration will be from about 5:1 to about 1:5. More preferably, the ration will be about 3:1 to about 1:3. Still more preferably, the ratio will be about 1:1.

U.S. Patent NO: 5,676,954 (which is herein incorporated by reference) reports on the injection of genetic material, complexed with cationic liposomes carriers, into mice. U.S. Patent Nos. 4,897,355, 4,946,787, 5,049,386, 5,459,127, 5,589,466, 5,693,622, 5,580,859, 5,703,055, and international publication NO: WO 94/9469 (which are herein incorporated by reference) provide cationic lipids for use in transfecting DNA into cells and mammals. U.S. Patent Nos. 5,589,466, 5,693,622, 5,580,859, 5,703,055, and international publication NO: WO 94/9469 (which are herein incorporated by reference) provide methods for delivering DNA-cationic lipid complexes to mammals.

In certain embodiments, cells are engineered, *ex vivo* or *in vivo*, using a retroviral particle containing RNA which comprises a sequence encoding polypeptides of the invention. Retroviruses from which the retroviral plasmid vectors may be derived include, but are not limited to, Moloney Murine Leukemia Virus, spleen necrosis virus, Rous sarcoma Virus, Harvey Sarcoma Virus, avian leukosis virus, gibbon ape leukemia virus, human immunodeficiency virus, Myeloproliferative Sarcoma Virus, and mammary tumor virus.

The retroviral plasmid vector is employed to transduce packaging cell lines to form producer cell lines. Examples of packaging cells which may be transfected include, but are not limited to, the PE501, PA317, R-2, R-AM, PA12, T19-14X, VT-19-17-H2, RCRE, RCRIP, GP+E-86, GP+envAm12, and DAN cell lines as described in Miller, Human Gene Therapy , 1:5-14 (1990), which is incorporated herein by reference in its entirety. The vector may transduce the packaging cells through any

means known in the art. Such means include, but are not limited to, electroporation, the use of liposomes, and $CaPO_4$ precipitation. In one alternative, the retroviral plasmid vector may be encapsulated into a liposome, or coupled to a lipid, and then administered to a host.

The producer cell line generates infectious retroviral vector particles which include polynucleotide encoding polypeptides of the invention. Such retroviral vector particles then may be employed, to transduce eukaryotic cells, either *in vitro* or *in vivo*. The transduced eukaryotic cells will express polypeptides of the invention.

In certain other embodiments, cells are engineered, *ex vivo* or *in vivo*, with polynucleotides of the invention contained in an adenovirus vector. Adenovirus can be manipulated such that it encodes and expresses polypeptides of the invention, and at the same time is inactivated in terms of its ability to replicate in a normal lytic viral life cycle. Adenovirus expression is achieved without integration of the viral DNA into the host cell chromosome, thereby alleviating concerns about insertional mutagenesis. Furthermore, adenoviruses have been used as live enteric vaccines for many years with an excellent safety profile (Schwartzet al., Am. Rev. Respir. Dis., 109:233-238 (1974)). Finally, adenovirus mediated gene transfer has been demonstrated in a number of instances including transfer of alpha-1-antitrypsin and CFTR to the lungs of cotton rats (Rosenfeld et al.,Science , 252:431-434 (1991); Rosenfeld et al., Cell, 68:143-155 (1992)). Furthermore, extensive studies to attempt to establish adenovirus as a causative agent in human cancer were uniformly negative (Green et al. Proc. Natl. Acad. Sci. USA , 76:6606 (1979)).

Suitable adenoviral vectors useful in the present invention are described, for example, in Kozarsky and Wilson, Curr. Opin. Genet. Devel., 3:499-503 (1993); Rosenfeld et al., Cell , 68:143-155 (1992); Engelhardt et al., Human Genet. Ther., 4:759-769 (1993); Yang et al., Nature Genet., 7:362-369 (1994); Wilson et al., Nature , 365:691-692 (1993); and U.S. Patent NO: 5,652,224, which are herein incorporated by reference. For example, the adenovirus vector Ad2 is useful and can be grown in human 293 cells. These cells contain the E1 region of adenovirus and constitutively express Ela and Elb, which complement the defective adenoviruses by providing the products of the genes deleted from the vector. In addition to Ad2, other

varieties of adenovirus (e.g., Ad3, Ad5, and Ad7) are also useful in the present invention.

Preferably, the adenoviruses used in the present invention are replication deficient. Replication deficient adenoviruses require the aid of a helper virus and/or packaging cell line to form infectious particles. The resulting virus is capable of infecting cells and can express a polynucleotide of interest which is operably linked to a promoter, but cannot replicate in most cells. Replication deficient adenoviruses may be deleted in one or more of all or a portion of the following genes: E1a, E1b, E3, E4, E2a, or L1 through L5.

In certain other embodiments, the cells are engineered, *ex vivo* or *in vivo*, using an adeno-associated virus (AAV). AAVs are naturally occurring defective viruses that require helper viruses to produce infectious particles (Muzyczka, Curr. Topics in Microbiol. Immunol., 158:97 (1992)). It is also one of the few viruses that may integrate its DNA into non-dividing cells. Vectors containing as little as 300 base pairs of AAV can be packaged and can integrate, but space for exogenous DNA is limited to about 4.5 kb. Methods for producing and using such AAVs are known in the art. See, for example, U.S. Patent Nos. 5,139,941, 5,173,414, 5,354,678, 5,436,146, 5,474,935, 5,478,745, and 5,589,377.

For example, an appropriate AAV vector for use in the present invention will include all the sequences necessary for DNA replication, encapsidation, and host-cell integration. The polynucleotide construct containing polynucleotides of the invention is inserted into the AAV vector using standard cloning methods, such as those found in Sambrook et al., Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Press (1989). The recombinant AAV vector is then transfected into packaging cells which are infected with a helper virus, using any standard technique, including lipofection, electroporation, calcium phosphate precipitation, etc. Appropriate helper viruses include adenoviruses, cytomegaloviruses, vaccinia viruses, or herpes viruses. Once the packaging cells are transfected and infected, they will produce infectious AAV viral particles which contain the polynucleotide construct of the invention. These viral particles are then used to transduce eukaryotic cells, either *ex vivo* or *in vivo*. The transduced cells will contain the polynucleotide construct integrated into its genome, and will express the desired gene product.

Another method of gene therapy involves operably associating heterologous control regions and endogenous polynucleotide sequences (e.g. encoding the polypeptide sequence of interest) via homologous recombination (see, e.g., U.S. Patent NO: 5,641,670, issued June 24, 1997; International Publication NO: WO 96/29411, published September 26, 1996; International Publication NO: WO 94/12650, published August 4, 1994; Koller et al., Proc. Natl. Acad. Sci. USA, 86:8932-8935 (1989); and Zijlstra et al., Nature, 342:435-438 (1989). This method involves the activation of a gene which is present in the target cells, but which is not normally expressed in the cells, or is expressed at a lower level than desired.

Polynucleotide constructs are made, using standard techniques known in the art, which contain the promoter with targeting sequences flanking the promoter. Suitable promoters are described herein. The targeting sequence is sufficiently complementary to an endogenous sequence to permit homologous recombination of the promoter-targeting sequence with the endogenous sequence. The targeting sequence will be sufficiently near the 5′ end of the desired endogenous polynucleotide sequence so the promoter will be operably linked to the endogenous sequence upon homologous recombination.

The promoter and the targeting sequences can be amplified using PCR. Preferably, the amplified promoter contains distinct restriction enzyme sites on the 5′ and 3′ ends. Preferably, the 3′ end of the first targeting sequence contains the same restriction enzyme site as the 5′ end of the amplified promoter and the 5′ end of the second targeting sequence contains the same restriction site as the 3′ end of the amplified promoter. The amplified promoter and targeting sequences are digested and ligated together.

The promoter-targeting sequence construct is delivered to the cells, either as naked polynucleotide, or in conjunction with transfection-facilitating agents, such as liposomes, viral sequences, viral particles, whole viruses, lipofection, precipitating agents, etc., described in more detail above. The P promoter-targeting sequence can be delivered by any method, included direct needle injection, intravenous injection, topical administration, catheter infusion, particle accelerators, etc. The methods are described in more detail below.

The promoter-targeting sequence construct is taken up by cells. Homologous recombination between the construct and the endogenous sequence takes place, such that an endogenous sequence is placed under the control of the promoter. The promoter then drives the expression of the endogenous sequence.

The polynucleotides encoding polypeptides of the present invention may be administered along with other polynucleotides encoding other angiongenic proteins. Angiogenic proteins include, but are not limited to, acidic and basic fibroblast growth factors, VEGF-1, VEGF-2 (VEGF-C), VEGF-3 (VEGF-B), epidermal growth factor alpha and beta, platelet-derived endothelial cell growth factor, platelet-derived growth factor, tumor necrosis factor alpha, hepatocyte growth factor, insulin like growth factor, colony stimulating factor, macrophage colony stimulating factor, granulocyte/macrophage colony stimulating factor, and nitric oxide synthase.

Preferably, the polynucleotide encoding a polypeptide of the invention contains a secretory signal sequence that facilitates secretion of the protein. Typically, the signal sequence is positioned in the coding region of the polynucleotide to be expressed towards or at the 5′ end of the coding region. The signal sequence may be homologous or heterologous to the polynucleotide of interest and may be homologous or heterologous to the cells to be transfected. Additionally, the signal sequence may be chemically synthesized using methods known in the art.

Any mode of administration of any of the above-described polynucleotides constructs can be used so long as the mode results in the expression of one or more molecules in an amount sufficient to provide a therapeutic effect. This includes direct needle injection, systemic injection, catheter infusion, biolistic injectors, particle accelerators (i.e., “gene guns”), gelfoam sponge depots, other commercially available depot materials, osmotic pumps (e.g., Alza minipumps), oral or suppositorial solid (tablet or pill) pharmaceutical formulations, and decanting or topical applications during surgery. For example, direct injection of naked calcium phosphate-precipitated plasmid into rat liver and rat spleen or a protein-coated plasmid into the portal vein has resulted in gene expression of the foreign gene in the rat livers. (Kaneda et al., Science, 243:375 (1989)).

A preferred method of local administration is by direct injection. Preferably, a recombinant molecule of the present invention complexed with a delivery vehicle is

administered by direct injection into or locally within the area of arteries. Administration of a composition locally within the area of arteries refers to injecting the composition centimeters and preferably, millimeters within arteries.

Another method of local administration is to contact a polynucleotide construct of the present invention in or around a surgical wound. For example, a patient can undergo surgery and the polynucleotide construct can be coated on the surface of tissue inside the wound or the construct can be injected into areas of tissue inside the wound.

Therapeutic compositions useful in systemic administration, include recombinant molecules of the present invention complexed to a targeted delivery vehicle of the present invention. Suitable delivery vehicles for use with systemic administration comprise liposomes comprising ligands for targeting the vehicle to a particular site.

Preferred methods of systemic administration, include intravenous injection, aerosol, oral and percutaneous (topical) delivery. Intravenous injections can be performed using methods standard in the art. Aerosol delivery can also be performed using methods standard in the art (see, for example, Stribling et al., Proc. Natl. Acad. Sci. USA , 189:11277-11281 (1992), which is incorporated herein by reference). Oral delivery can be performed by complexing a polynucleotide construct of the present invention to a carrier capable of withstanding degradation by digestive enzymes in the gut of an animal. Examples of such carriers, include plastic capsules or tablets, such as those known in the art. Topical delivery can be performed by mixing a polynucleotide construct of the present invention with a lipophilic reagent (e.g., DMSO) that is capable of passing into the skin.

Determining an effective amount of substance to be delivered can depend upon a number of factors including, for example, the chemical structure and biological activity of the substance, the age and weight of the animal, the precise condition requiring treatment and its severity, and the route of administration. The frequency of treatments depends upon a number of factors, such as the amount of polynucleotide constructs administered per dose, as well as the health and history of the subject. The precise amount, number of doses, and timing of doses will be determined by the attending physician or veterinarian. Therapeutic compositions of

the present invention can be administered to any animal, preferably to mammals and birds. Preferred mammals include humans, dogs, cats, mice, rats, rabbits sheep, cattle, horses and pigs, with humans being particularly

Biological Activities

The polynucleotides or polypeptides, or agonists or antagonists of the present invention can be used in assays to test for one or more biological activities. If these polynucleotides and polypeptides do exhibit activity in a particular assay, it is likely that these molecules may be involved in the diseases associated with the biological activity. Thus, the polynucleotides or polypeptides, or agonists or antagonists could be used to treat the associated disease.

The present invention encompasses methods of preventing, treating, diagnosing, or ameliorating a disease or disorder. In preferred embodiments, the present invention encompasses a method of treating a disease or disorder listed in the "Preferred Indications" column of Table 1C; comprising administering to a patient in which such treatment, prevention, or amelioration is desired a protein, nucleic acid, or antibody of the invention (or fragment or variant thereof) in an amount effective to treat, prevent, diagnose, or ameliorate the disease or disorder. The first and seccond columns of Table 1C show the "Gene No." and "cDNA Clone ID No.", respectively, indicating certain nucleic acids and proteins (or antibodies against the same) of the invention (including polynucleotide, polypeptide, and antibody fragments or variants thereof) that may be used in preventing, treating, diagnosing, or ameliorating the disease(s) or disorder(s) indicated in the corresponding row in Column 3 of Table 1C.

In another embodiment, the present invention also encompasses methods of preventing, treating, diagnosing, or ameliorating a disease or disorder listed in the "Preferred Indications" column of Table 1C; comprising administering to a patient combinations of the proteins, nucleic acids, or antibodies of the invention (or fragments or variants thereof), sharing similar indications as shown in the corresponding rows in Column 3 of Table 1C.

The "Preferred Indication" column describes diseases, disorders, and/or conditions that may be treated, prevented, diagnosed, or ameliorated by a protein, nucleic acid, or antibody of the invention (or fragment or variant thereof).

The recitation of "Cancer" in the "Preferred Indication" column indicates that the corresponding nucleic acid and protein, or antibody against the same, of the invention (or fragment or variant thereof) may be used for example, to diagnose, treat, prevent, and/or ameliorate diseases and/or disorders relating to neoplastic diseases (e.g., leukemias, cancers, and/or as described below under "Hyperproliferative Disorders").

In specific embodiments, a protein, nucleic acid, or antibody of the invention (or fragment or variant thereof) having a "Cancer" recitation in the "Preferred Indication" column of Table 1C may be used for example, to diagnose, treat, prevent, and/or ameliorate a neoplasm located in a tissue selected from the group consisting of: colon, abdomen, bone, breast, digestive system, liver, pancreas, prostate, peritoneum, lung, blood (e.g., leukemia), endocrine glands (adrenal, parathyroid, pituitary, testicles, ovary, thymus, thyroid), uterus, eye, head and neck, nervous (central and peripheral), lymphatic system, pelvic, skin, soft tissue, spleen, thoracic, and urogenital.

In specific embodiments, a protein, nucleic acid, or antibody of the invention (or fragment or variant thereof) having a "Cancer" recitation in the "Preferred Indication" column of Table 1C, may be used for example, to diagnose, treat, prevent, and/or ameliorate a pre-neoplastic condition, selected from the group consisting of: hyperplasia (e.g., endometrial hyperplasia and/or as described in the section entitled "Hyperproliferative Disorders"), metaplasia (e.g., connective tissue metaplasia, atypical metaplasia, and/or as described in the section entitled "Hyperproliferative Disorders"), and/or dysplasia (e.g., cervical dysplasia, and bronchopulmonary dysplasia).

In another specific embodiment, a protein, nucleic acid, or antibody of the invention (or fragment or variant thereof) having a "Cancer" recitation in the "Preferred Indication" column of Table 1C, may be used for example, to diagnose, treat, prevent, and/or ameliorate a benign dysproliferative disorder selected from the group consisting of: benign tumors, fibrocystic conditions, tissue hypertrophy, and/or as described in the section entitled "Hyperproliferative Disorders".

The recitation of "Immune/Hematopoietic" in the "Preferred Indication" column indicates that the corresponding nucleic acid and protein, or antibody against

the same, of the invention (or fragment or variant thereof), may be used for example, to diagnose, treat, prevent, and/or ameliorate diseases and/or disorders relating to neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Immune Activity" "Cardiovascular Disorders" and/or "Blood-Related Disorders"), and infections (e.g., as described below under "Infectious Disease").

In specific embodiments, a protein, nucleic acid, or antibody of the invention (or fragment or variant thereof) having the "Immune/Hematopoietic" recitation in the "Preferred Indication" column of Table 1C, may be used for example, to diagnose, treat, prevent, and/or ameliorate a disease or disorder selected from the group consisting of: anemia, pancytopenia, leukopenia, thrombocytopenia, leukemias, Hodgkin's disease, non-Hodgkin's lymphoma, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, asthma, AIDS, autoimmune disease, rheumatoid arthritis, granulomatous disease, immune deficiency, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, immune reactions to transplanted organs and tissues, systemic lupus erythematosis, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and allergies.

The recitation of "Reproductive" in the "Preferred Indication" column indicates that the corresponding nucleic acid and protein, or antibody against the same, of the invention (or fragment or variant thereof), may be used for example, to diagnose, treat, prevent, and/or ameliorate diseases and/or disorders relating to neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), and disorders of the reproductive system (e.g., as described below under "Reproductive System Disorders").

In specific embodiments, a protein, nucleic acid, or antibody of the invention (or fragment or variant thereof) having a "Reproductive" recitation in the "Preferred Indication" column of Table 1C, may be used for example, to diagnose, treat, prevent, and/or ameliorate a disease or disorder selected from the group consisting of: cryptorchism, prostatitis, inguinal hernia, varicocele, leydig cell tumors, verrucous carcinoma, prostatitis, malacoplakia, Peyronie's disease, penile carcinoma, squamous cell hyperplasia, dysmenorrhea, ovarian adenocarcinoma, Turner's syndrome,

mucopurulent cervicitis, Sertoli-leydig tumors, ovarian cancer, uterine cancer, pelvic inflammatory disease, testicular cancer, prostate cancer, Klinefelter's syndrome, Young's syndrome, premature ejaculation, diabetes mellitus, cystic fibrosis, Kartagener's syndrome, testicular atrophy, testicular feminization, anorchia, ectopic testis, epididymitis, orchitis, gonorrhea, syphilis, testicular torsion, vasitis nodosa, germ cell tumors, stromal tumors, dysmenorrhea, retroverted uterus, endometriosis, fibroids, adenomyosis, anovulatory bleeding, amenorrhea, Cushing's syndrome, hydatidiform moles, Asherman's syndrome, premature menopause, precocious puberty, uterine polyps, dysfunctional uterine bleeding, cervicitis, chronic cervicitis, mucopurulent cervicitis, cervical dysplasia, cervical polyps, Nabothian cysts, cervical erosion, cervical incompetence, cervical neoplasms, pseudohermaphroditism, and premenstrual syndrome.

The recitation of "Musculoskeletal" in the "Preferred Indication" column indicates that the corresponding nucleic acid and protein, or antibody against the same, of the invention (or fragment or variant thereof), may be used for example, to diagnose, treat, prevent, and/or ameliorate diseases and/or disorders relating to neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), and disorders of the immune system (e.g., as described below under "Immune Activity").

In specific embodiments, a protein, nucleic acid, or antibody of the invention (or fragment or variant thereof) having a "Musculoskeletal" recitation in the "Preferred Indication" column of Table 1C, may be used for example, to diagnose, treat, prevent, and/or ameliorate a disease or disorder selected from the group consisting of: bone cancers (e.g., osteochondromas, benign chondromas, chondroblastoma, chondromyxoid fibromas, osteoid osteomas, giant cell tumors, multiple myeloma, osteosarcomas), Paget's Disease, rheumatoid arthritis, systemic lupus erythematosus, osteomyelitis, Lyme Disease, gout, bursitis, tendonitis, osteoporosis, osteoarthritis, muscular dystrophy, mitochondrial myopathy, cachexia, and multiple sclerosis.

The recitation of "Cardiovascular" in the "Preferred Indication" column indicates that the corresponding nucleic acid and protein, or antibody against the same, of the invention (or fragment or variant thereof), may be used for example, to

diagnose, treat, prevent, and/or ameliorate diseases and/or disorders relating to neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), and disorders of the cardiovascular system (e.g., as described below under "Cardiovascular Disorders").

In specific embodiments, a protein, nucleic acid, or antibody of the invention (or fragment or variant thereof) having a "Cardiovascular" recitation in the "Preferred Indication" column of Table 1C, may be used for example, to diagnose, treat, prevent, and/or ameliorate a disease or disorder selected from the group consisting of: myxomas, fibromas, rhabdomyomas, cardiovascular abnormalities (e.g., congenital heart defects, cerebral arteriovenous malformations, septal defects), heart disease (e.g., heart failure, congestive heart disease, arrhythmia, tachycardia, fibrillation, pericardial Disease, endocarditis), cardiac arrest, heart valve disease (e.g., stenosis, regurgitation, prolapse), vascular disease (e.g., hypertension, coronary artery disease, angina, aneurysm, arteriosclerosis, peripheral vascular disease), hyponatremia, hypernatremia, hypokalemia, and hyperkalemia.

The recitation of "Mixed Fetal" in the "Preferred Indication" column indicates that the corresponding nucleic acid and protein, or antibody against the same, of the invention (or fragment or variant thereof), may be used for example, to diagnose, treat, prevent, and/or ameliorate diseases and/or disorders relating to neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders").

In specific embodiments, a protein, nucleic acid, or antibody of the invention (or fragment or variant thereof) having a "Mixed Fetal" recitation in the "Preferred Indication" column of Table 1C, may be used for example, to diagnose, treat, prevent, and/or ameliorate a disease or disorder selected from the group consisting of: spina bifida, hydranencephaly, neurofibromatosis, fetal alcohol syndrome, diabetes mellitus, PKU, Down's syndrome, Patau syndrome, Edwards syndrome, Turner syndrome, Apert syndrome, Carpenter syndrome, Conradi syndrome, Crouzon syndrome, cutis laxa, Cornelia de Lange syndrome, Ellis-van Creveld syndrome, Holt-Oram syndrome, Kartagener syndrome, Meckel-Gruber syndrome, Noonan syndrome, Pallister-Hall syndrome, Rubinstein-Taybi syndrome, Scimitar syndrome, Smith-Lemli-Opitz syndrome, thromocytopenia-absent radius (TAR) syndrome, Treacher Collins syndrome, Williams syndrome, Hirschsprung's disease, Meckel's

diverticulum, polycystic kidney disease, Turner's syndrome, and gonadal dysgenesis, Klippel-Feil syndrome, Ostogenesis imperfecta, muscular dystrophy, Tay-Sachs disease, Wilm's tumor, neuroblastoma, and retinoblastoma.

The recitation of "Excretory" in the "Preferred Indication" column indicates that the corresponding nucleic acid and protein, or antibody against the same, of the invention (or fragment or variant thereof), may be used for example, to diagnose, treat, prevent, and/or ameliorate diseases and/or disorders relating to neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders") and renal disorders (e.g., as described below under "Renal Disorders").

In specific embodiments, a protein, nucleic acid, or antibody of the invention (or fragment or variant thereof) having a "Excretory" recitation in the "Preferred Indication" column of Table 1C, may be used for example, to diagnose, treat, prevent, and/or ameliorate a disease or disorder selected from the group consisting of: bladder cancer, prostate cancer, benign prostatic hyperplasia, bladder disorders (e.g., urinary incontinence, urinary retention, urinary obstruction, urinary tract Infections, interstitial cystitis, prostatitis, neurogenic bladder, hematuria), renal disorders (e.g., hydronephrosis, proteinuria, renal failure, pyelonephritis, urolithiasis, reflux nephropathy, and unilateral obstructive uropathy).

The recitation of "Neural/Sensory" in the "Preferred Indication" column indicates that the corresponding nucleic acid and protein, or antibody against the same, of the invention (or fragment or variant thereof), may be used for example, to diagnose, treat, prevent, and/or ameliorate diseases and/or disorders relating to neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders") and diseases or disorders of the nervous system (e.g., as described below under "Neural Activity and Neurological Diseases").

In specific embodiments, a protein, nucleic acid, or antibody of the invention (or fragment or variant thereof) having a "Neural/Sensory" recitation in the "Preferred Indication" column of Table 1C, may be used for example, to diagnose, treat, prevent, and/or ameliorate a disease or disorder selected from the group consisting of: brain cancer (e.g., brain stem glioma, brain tumors, central nervous system (Primary) lymphoma, central nervous system lymphoma, cerebellar astrocytoma, and cerebral astrocytoma, neurodegenerative disorders (e.g., Alzheimer's Disease, Creutzfeldt-

Jakob Disease, Parkinson's Disease, and Idiopathic Presenile Dementia), encephalomyelitis, cerebral malaria, meningitis, metabolic brain diseases (e.g., phenylketonuria and pyruvate carboxylase deficiency), cerebellar ataxia, ataxia telangiectasia, and AIDS Dementia Complex, schizophrenia, attention deficit disorder, hyperactive attention deficit disorder, autism, and obsessive compulsive disorders.

The recitation of "Respiratory" in the "Preferred Indication" column indicates that the corresponding nucleic acid and protein, or antibody against the same, of the invention (or fragment or variant thereof), may be used for example, to diagnose, treat, prevent, and/or ameliorate diseases and/or disorders relating to neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders") and diseases or disorders of the respiratory system (e.g., as described below under "Respiratory Disorders").

In specific embodiments, a protein, nucleic acid, or antibody of the invention (or fragment or variant thereof) having a "Respiratory" recitation in the "Preferred Indication" column of Table 1C, may be used for example, to diagnose, treat, prevent, and/or ameliorate a disease or disorder selected from the group consisting of: cancers of the respiratory system such as larynx cancer, pharynx cancer, trachea cancer, epiglottis cancer, lung cancer, squamous cell carcinomas, small cell (oat cell) carcinomas, large cell carcinomas, and adenocarcinomas. Allergic reactions, cystic fibrosis, sarcoidosis, histiocytosis X, infiltrative lung diseases (e.g., pulmonary fibrosis and lymphoid interstitial pneumonia), obstructive airway diseases (e.g., asthma, emphysema, chronic or acute bronchitis), occupational lung diseases (e.g., silicosis and asbestosis), pneumonia, and pleurisy.

The recitation of "Endocrine" in the "Preferred Indication" column indicates that the corresponding nucleic acid and protein, or antibody against the same, of the invention (or fragment or variant thereof), may be used for example, to diagnose, treat, prevent, and/or ameliorate diseases and/or disorders relating to neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders") and diseases or disorders of the respiratory system (e.g., as described below under "Respiratory Disorders"), renal disorders (e.g., as described below under "Renal Disorders"), and

disorders of the endocrine system (e.g., as described below under "Endocrine Disorders".

In specific embodiments, a protein, nucleic acid, or antibody of the invention (or fragment or variant thereof) having an "Endocrine" recitation in the "Preferred Indication" column of Table 1C, may be used for example, to diagnose, treat, prevent, and/or ameliorate a disease or disorder selected from the group consisting of: cancers of endocrine tissues and organs (e.g., cancers of the hypothalamus, pituitary gland, thyroid gland, parathyroid glands, pancreas, adrenal glands, ovaries, and testes), diabetes (e.g., diabetes insipidus, type I and type II diabetes mellitus), obesity, disorders related to pituitary glands (e.g., hyperpituitarism, hypopituitarism, and pituitary dwarfism), hypothyroidism, hyperthyroidism, goiter, reproductive disorders (e.g. male and female infertility), disorders related to adrenal glands (e.g., Addison's Disease, corticosteroid deficiency, and Cushing's Syndrome), kidney cancer (e.g., hypernephroma, transitional cell cancer, and Wilm's tumor), diabetic nephropathy, interstitial nephritis, polycystic kidney disease, glomerulonephritis (e.g., IgM mesangial proliferative glomerulonephritis and glomerulonephritis caused by autoimmune disorders; such as Goodpasture's syndrome), and nephrocalcinosis.

The recitation of "Digestive" in the "Preferred Indication" column indicates that the corresponding nucleic acid and protein, or antibody against the same, of the invention (or fragment or variant thereof), may be used for example, to diagnose, treat, prevent, and/or ameliorate diseases and/or disorders relating to neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders") and diseases or disorders of the gastrointestinal system (e.g., as described below under "Gastrointestinal Disorders".

In specific embodiments, a protein, nucleic acid, or antibody of the invention (or fragment or variant thereof) having a "Digestive" recitation in the "Preferred Indication" column of Table 1C, may be used for example, to diagnose, treat, prevent, and/or ameliorate a disease or disorder selected from the group consisting of: ulcerative colitis, appendicitis, Crohn's disease, hepatitis, hepatic encephalopathy, portal hypertension, cholelithiasis, cancer of the digestive system (e.g., biliary tract cancer, stomach cancer, colon cancer, gastric cancer, pancreatic cancer, cancer of the bile duct, tumors of the colon (e.g., polyps or cancers), and cirrhosis), pancreatitis,

ulcerative disease, pyloric stenosis, gastroenteritis, gastritis, gastric atropy, benign tumors of the duodenum, distension, irritable bowel syndrome, malabsorption, congenital disorders of the small intestine, bacterial and parasitic infection, megacolon, Hirschsprung's disease, aganglionic megacolon, acquired megacolon, colitis, anorectal disorders (e.g., anal fistulas, hemorrhoids), congenital disorders of the liver (e.g., Wilson's disease, hemochromatosis, cystic fibrosis, biliary atresia, and alpha1-antitrypsin deficiency), portal hypertension, cholelithiasis, and jaundice.

The recitation of "Connective/Epithelial" in the "Preferred Indication" column indicates that the corresponding nucleic acid and protein, or antibody against the same, of the invention (or fragment or variant thereof), may be used for example, to diagnose, treat, prevent, and/or ameliorate diseases and/or disorders relating to neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), cellular and genetic abnormalities (e.g., as described below under "Diseases at the Cellular Level "), angiogenesis (e.g., as described below under "Anti-Angiogenesis Activity "), and or to promote or inhibit regeneration (e.g., as described below under "Regeneration "), and wound healing (e.g., as described below under "Wound Healing and Epithelial Cell Proliferation").

In specific embodiments, a protein, nucleic acid, or antibody of the invention (or fragment or variant thereof) having a "Connective/Epithelial" recitation in the "Preferred Indication" column of Table 1C, may be used for example, to diagnose, treat, prevent, and/or ameliorate a disease or disorder selected from the group consisting of: connective tissue metaplasia, mixed connective tissue disease, focal epithelial hyperplasia, epithelial metaplasia, mucoepithelial dysplasia, graft v. host disease, polymyositis, cystic hyperplasia, cerebral dysplasia, tissue hypertrophy, Alzheimer's disease, lymphoproliferative disorder, Waldenstron's macroglobulinemia, Crohn's disease, pernicious anemia, idiopathic Addison's disease, glomerulonephritis, bullous pemphigoid, Sjogren's syndrome, diabetes mellitus, cystic fibrosis, osteoblastoma, osteoclastoma, osteosarcoma, chondrosarcoma, osteoporosis, osteocarthritis, periodontal disease, wound healing, relapsing polychondritis, vasculitis, polyarteritis nodosa, Wegener's granulomatosis, cellulitis, rheumatoid arthritis, psoriatic arthritis, discoid lupus erythematosus, systemic lupus erythematosus, scleroderma, CREST syndrome, Sjogren's syndrome, polymyositis,

dermatomyositis, mixed connective tissue disease, relapsing polychondritis, vasculitis, Henoch-Schonlein syndrome, erythema nodosum, polyarteritis nodosa, temporal (giant cell) arteritis, Takayasu's arteritis, Wegener's granulomatosis, Reiter's syndrome, Behcet's syndrome, ankylosing spondylitis, cellulitis, keloids, Ehler Danlos syndrome, Marfan syndrome, pseudoxantoma elasticum, osteogenese imperfecta, chondrodysplasias, epidermolysis bullosa, Alport syndrome, and cutis laxa.

Moreover, polynucleotides, translation products and antibodies corresponding to this gene may be useful for the diagnosis, prognosis, prevention, and/or treatment of diseases and/or disorders associated with the following systems.

Immune Activity

Polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention may be useful in treating, preventing, diagnosing and/or prognosing diseases, disorders, and/or conditions of the immune system, by, for example, activating or inhibiting the proliferation, differentiation, or mobilization (chemotaxis) of immune cells. Immune cells develop through a process called hematopoiesis, producing myeloid (platelets, red blood cells, neutrophils, and macrophages) and lymphoid (B and T lymphocytes) cells from pluripotent stem cells. The etiology of these immune diseases, disorders, and/or conditions may be genetic, somatic, such as cancer and some autoimmune diseases, acquired (e.g., by chemotherapy or toxins), or infectious. Moreover, polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention can be used as a marker or detector of a particular immune system disease or disorder.

In another embodiment, a polypeptide of the invention, or polynucleotides, antibodies, agonists, or antagonists corresponding to that polypeptide, may be used to treat diseases and disorders of the immune system and/or to inhibit or enhance an immune response generated by cells associated with the tissue(s) in which the polypeptide of the invention is expressed, including one, two, three, four, five, or more tissues disclosed in Table 1B, column 8 (Tissue Distribution Library Code).

Polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention may be useful in treating, preventing, diagnosing, and/or prognosing immunodeficiencies, including both congenital and acquired immunodeficiencies. Examples of B cell immunodeficiencies in which immunoglobulin levels B cell function and/or B cell numbers are decreased include: X-linked agammaglobulinemia (Bruton's disease), X-linked infantile agammaglobulinemia, X-linked immunodeficiency with hyper IgM, non X-linked immunodeficiency with hyper IgM, X-linked lymphoproliferative syndrome (XLP), agammaglobulinemia including congenital and acquired agammaglobulinemia, adult onset agammaglobulinemia, late-onset agammaglobulinemia, dysgammaglobulinemia, hypogammaglobulinemia, unspecified hypogammaglobulinemia, recessive agammaglobulinemia (Swiss type), Selective IgM deficiency, selective IgA deficiency, selective IgG subclass deficiencies, IgG subclass deficiency (with or without IgA deficiency), Ig deficiency with increased IgM, IgG and IgA deficiency with increased IgM, antibody deficiency with normal or elevated Igs, Ig heavy chain deletions, kappa chain deficiency, B cell lymphoproliferative disorder (BLPD), common variable immunodeficiency (CVID), common variable immunodeficiency (CVI) (acquired), and transient hypogammaglobulinemia of infancy.

In specific embodiments, ataxia-telangiectasia or conditions associated with ataxia-telangiectasia are treated, prevented, diagnosed, and/or prognosing using the polypeptides or polynucleotides of the invention, and/or agonists or antagonists thereof.

Examples of congenital immunodeficiencies in which T cell and/or B cell function and/or number is decreased include, but are not limited to: DiGeorge anomaly, severe combined immunodeficiencies (SCID) (including, but not limited to, X-linked SCID, autosomal recessive SCID, adenosine deaminase deficiency, purine nucleoside phosphorylase (PNP) deficiency, Class II MHC deficiency (Bare lymphocyte syndrome), Wiskott-Aldrich syndrome, and ataxia telangiectasia), thymic hypoplasia, third and fourth pharyngeal pouch syndrome, 22q11.2 deletion, chronic mucocutaneous candidiasis, natural killer cell deficiency (NK), idiopathic CD4+ T-lymphocytopenia, immunodeficiency with predominant T cell defect (unspecified), and unspecified immunodeficiency of cell mediated immunity.

In specific embodiments, DiGeorge anomaly or conditions associated with DiGeorge anomaly are treated, prevented, diagnosed, and/or prognosed using polypeptides or polynucleotides of the invention, or antagonists or agonists thereof.

Other immunodeficiencies that may be treated, prevented, diagnosed, and/or prognosed using polypeptides or polynucleotides of the invention, and/or agonists or antagonists thereof, include, but are not limited to, chronic granulomatous disease, Chédiak-Higashi syndrome, myeloperoxidase deficiency, leukocyte glucose-6-phosphate dehydrogenase deficiency, X-linked lymphoproliferative syndrome (XLP), leukocyte adhesion deficiency, complement component deficiencies (including C1, C2, C3, C4, C5, C6, C7, C8 and/or C9 deficiencies), reticular dysgenesis, thymic alymphoplasia-aplasia, immunodeficiency with thymoma, severe congenital leukopenia, dysplasia with immunodeficiency, neonatal neutropenia, short limbed dwarfism, and Nezelof syndrome-combined immunodeficiency with Igs.

In a preferred embodiment, the immunodeficiencies and/or conditions associated with the immunodeficiencies recited above are treated, prevented, diagnosed and/or prognosed using polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention.

In a preferred embodiment polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention could be used as an agent to boost immunoresponsiveness among immunodeficient individuals. In specific embodiments, polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention could be used as an agent to boost immunoresponsiveness among B cell and/or T cell immunodeficient individuals.

The polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention may be useful in treating, preventing, diagnosing and/or prognosing autoimmune disorders. Many autoimmune disorders result from inappropriate recognition of self as foreign material by immune cells. This inappropriate recognition results in an immune response leading to the destruction of the host tissue. Therefore, the administration of polynucleotides and polypeptides of the invention that can inhibit an immune response, particularly the proliferation, differentiation, or chemotaxis of T-cells, may be an effective therapy in preventing autoimmune disorders.

Autoimmune diseases or disorders that may be treated, prevented, diagnosed and/or prognosed by polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention include, but are not limited to, one or more of the following: systemic lupus erythematosus, rheumatoid arthritis, ankylosing spondylitis, multiple sclerosis, autoimmune thyroiditis, Hashimoto's thyroiditis, autoimmune hemolytic anemia, hemolytic anemia, thrombocytopenia, autoimmune thrombocytopenia purpura, autoimmune neonatal thrombocytopenia, idiopathic thrombocytopenia purpura, purpura (e.g., Henloch-Scoenlein purpura), autoimmunocytopenia, Goodpasture's syndrome, Pemphigus vulgaris, myasthenia gravis, Grave's disease (hyperthyroidism), and insulin-resistant diabetes mellitus.

Additional disorders that are likely to have an autoimmune component that may be treated, prevented, and/or diagnosed with the compositions of the invention include, but are not limited to, type II collagen-induced arthritis, antiphospholipid syndrome, dermatitis, allergic encephalomyelitis, myocarditis, relapsing polychondritis, rheumatic heart disease, neuritis, uveitis ophthalmia, polyendocrinopathies, Reiter's Disease, Stiff-Man Syndrome, autoimmune pulmonary inflammation, autism, Guillain-Barre Syndrome, insulin dependent diabetes mellitus, and autoimmune inflammatory eye disorders.

Additional disorders that are likely to have an autoimmune component that may be treated, prevented, diagnosed and/or prognosed with the compositions of the invention include, but are not limited to, scleroderma with anti-collagen antibodies (often characterized, e.g., by nucleolar and other nuclear antibodies), mixed connective tissue disease (often characterized, e.g., by antibodies to extractable nuclear antigens (e.g., ribonucleoprotein)), polymyositis (often characterized, e.g., by nonhistone ANA), pernicious anemia (often characterized, e.g., by antiparietal cell, microsomes, and intrinsic factor antibodies), idiopathic Addison's disease (often characterized, e.g., by humoral and cell-mediated adrenal cytotoxicity, infertility (often characterized, e.g., by antispermatozoal antibodies), glomerulonephritis (often characterized, e.g., by glomerular basement membrane antibodies or immune complexes), bullous pemphigoid (often characterized, e.g., by IgG and complement in basement membrane), Sjogren's syndrome (often characterized, e.g., by multiple tissue antibodies, and/or a specific nonhistone ANA (SS-B)), diabetes mellitus (often

characterized, e.g., by cell-mediated and humoral islet cell antibodies), and adrenergic drug resistance (including adrenergic drug resistance with asthma or cystic fibrosis) (often characterized, e.g., by beta-adrenergic receptor antibodies).

Additional disorders that may have an autoimmune component that may be treated, prevented, diagnosed and/or prognosed with the compositions of the invention include, but are not limited to, chronic active hepatitis (often characterized, e.g., by smooth muscle antibodies), primary biliary cirrhosis (often characterized, e.g., by mitochondria antibodies), other endocrine gland failure (often characterized, e.g., by specific tissue antibodies in some cases), vitiligo (often characterized, e.g., by melanocyte antibodies), vasculitis (often characterized, e.g., by Ig and complement in vessel walls and/or low serum complement), post-MI (often characterized, e.g., by myocardial antibodies), cardiotomy syndrome (often characterized, e.g., by myocardial antibodies), urticaria (often characterized, e.g., by IgG and IgM antibodies to IgE), atopic dermatitis (often characterized, e.g., by IgG and IgM antibodies to IgE), asthma (often characterized, e.g., by IgG and IgM antibodies to IgE), and many other inflammatory, granulomatous, degenerative, and atrophic disorders.

In a preferred embodiment, the autoimmune diseases and disorders and/or conditions associated with the diseases and disorders recited above are treated, prevented, diagnosed and/or prognosed using for example, antagonists or agonists, polypeptides or polynucleotides, or antibodies of the present invention. In a specific preferred embodiment, rheumatoid arthritis is treated, prevented, and/or diagnosed using polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention.

In another specific preferred embodiment, systemic lupus erythematosus is treated, prevented, and/or diagnosed using polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention. In another specific preferred embodiment, idiopathic thrombocytopenia purpura is treated, prevented, and/or diagnosed using polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention.

In another specific preferred embodiment IgA nephropathy is treated, prevented, and/or diagnosed using polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention.

In a preferred embodiment, the autoimmune diseases and disorders and/or conditions associated with the diseases and disorders recited above are treated, prevented, diagnosed and/or prognosed using polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention

In preferred embodiments, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as a immunosuppressive agent(s).

Polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention may be useful in treating, preventing, prognosing, and/or diagnosing diseases, disorders, and/or conditions of hematopoietic cells. Polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention could be used to increase differentiation and proliferation of hematopoietic cells, including the pluripotent stem cells, in an effort to treat or prevent those diseases, disorders, and/or conditions associated with a decrease in certain (or many) types hematopoietic cells, including but not limited to, leukopenia, neutropenia, anemia, and thrombocytopenia. Alternatively, Polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention could be used to increase differentiation and proliferation of hematopoietic cells, including the pluripotent stem cells, in an effort to treat or prevent those diseases, disorders, and/or conditions associated with an increase in certain (or many) types of hematopoietic cells, including but not limited to, histiocytosis.

Allergic reactions and conditions, such as asthma (particularly allergic asthma) or other respiratory problems, may also be treated, prevented, diagnosed and/or prognosed using polypeptides, antibodies, or polynucleotides of the invention, and/or agonists or antagonists thereof. Moreover, these molecules can be used to treat, prevent, prognose, and/or diagnose anaphylaxis, hypersensitivity to an antigenic molecule, or blood group incompatibility.

Additionally, polypeptides or polynucleotides of the invention, and/or agonists or antagonists thereof, may be used to treat, prevent, diagnose and/or prognose IgE-mediated allergic reactions. Such allergic reactions include, but are not limited to, asthma, rhinitis, and eczema. In specific embodiments, polynucleotides,